

# Overview of COVID19 In Hypertension Patients

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## Abstract

**Introduction:** The coronavirus disease 2019 (COVID-19) is worldwide outbreak. Globally there are 21,159,730 reported confirmed cases and there is almost no country in the world that is not affected by COVID-19 (3). It is caused by severe acute respiratory syndrome coronavirus 2 respiratory syndrome coronavirus 2 (SARS-CoV-2) enter the cells through angiotensin converting enzyme 2 (ACE2) receptor that act as key regulator of blood pressure.

**Objective:** To summarize the most updated data on COVID-19 and hypertension

**Methodology:** A PubMed and UpToDate search was completed in Clinical Queries using the key terms 'COVID-19 in hypertension patients' and 'COVID-19'. The search strategy included meta-analyses, randomized controlled trials, clinical trials, observational studies, and reviews

**Result:** 1099 patients with confirmed COVID-19, of which the single highest risk factor of infection was hypertension reported in 15% of patients. Meta-analysis of six studies (1527) patients, hypertension was present in 17.1% of patients with the infection. The median age of SARS-CoV-2-positive patients who died was 78.5 years. significantly higher usage of ARBs in hypertensive patients with moderate COVID-19 disease than those with a severe and critical course of disease. There is no advantage to any group of medications within RAAS inhibitors. There are no data regarding the association between RAAS inhibitors and the outcome.

**Conclusion:** There is a relation between COVID-19 and HTN and need more data to be clarify weather HTN is isolated risk factor or as a reflection of ACEI or ARB. Age is associated with COVID19.

**Abbreviations:** COVID-19; Hypertension; ACE; ARB

## Introduction

The coronavirus disease 2019 (COVID-19) is worldwide outbreak (1). Globally there are 21,159,730 reported confirmed cases (2) and there is almost no country in the world that is not affected by COVID-19 (3). It is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection (4) a positive stranded RNA virus (5). It transmitted animal to person and person to person. During this outbreak person to person is the main mode of transmission. The transmission occurs through respiratory droplets; when a person with infection coughs or sneezes he or she can infect another close-range contact person (5) respiratory syndrome coronavirus 2 (SARS-CoV-2) enter the cells through angiotensin converting enzyme 2 (ACE2) receptor (6). It catalyzes the conversion of angiotensin II to angiotensin I (7) ACE2 receptor

act as key regulator of blood pressure. High or uncontrolled blood pressure cause the patient a preventable cardiovascular disease witch is a leading cause of morbidity and mortality globally (8) Alot of studies have been raising the question about the relation between COVID- 19 and hypertension. A lot of published article reviews, retrospectives and metaanalysis regard the association between COVID 19 and hypertension. Here, we summarize the most updated data on COVID-19 and hypertension.

## Hypertension

Hypertension defined as a systolic blood pressure (BP)  $\geq 130$  or diastolic BP  $\geq 80$  mm Hg by American collage academy (8). It is determined by at least two measurements in the clinic setting one

minute at least apart (10). Globally, 1 in 4 men and 1 in 5 women diagnosed with chronic HTN (11.12). Raised blood pressure is a major risk factor for chronic heart disease, stroke, and coronary heart disease. It is a global cause of mortality (13) (Table1).

**Table 1.**

Elevated	
SBP	120-129
DBP	<80
Hypertension	
Stage	
SBP	130-139
DBP	80-89
Stage	
SBP	≥140
DBP	≥ 90

Other complication of hypertension including heart failure, peripheral vascular disease, renal impairment, retinal hemorrhage, and visual impairment (14) hypertension symptomless so it consider a silent killer (15) Singh and Shikha summarized the hypertension risk factor in their study to : male, elderly, married subjects, upper socioeconomic status, illiterate, retirement , tobacco and alcohol consumption, overweight and obesity (15).

### The association of HTN and COVID-19

The concern about the relationship between hypertension and COVID19 was the concern of many studies. Since the pathogenesis of COVID19 interact with ACE2 receptors a one of the components of the renin-angiotensin system (RAS) (16) that paly rule in blood pressure regulation. Hypertension is the highest risk factor of COVID- 19 patients regard Guan et al study of 1099 patient with confirmed COVID-19 (17). Zhang et al. result that 30% of 140 patients of COVID19 suffer from HTN (18). Although Kulkarni et al comment on Guan et al and Zhang et al with unknown timing of hypertension diagnosis, antihypertensive medication usage and adherence and control of hypertension and since the rapidity of the data collection in the current climate it has have limitations. (19) Meta-analysis of Li, B et al on 1527 COVID 19 patient found 17.1% suffer from HTN and there are suffering from COVID-19 severity by 2 fold than non HTN (20) and the most comorbidities in COVID19 is hypertension witch represent (30%) of the patients (21) On other hand - multivariate analysis of Huang et al failed to show that hypertension was an independent risk factor for COVID-19 mortality or severity .(22) In Wu C st al study (32.8%) of the patients had comorbidities . hypertension represent [19.4%] of them, then diabetes 10.9%, liver disease [3.5%], nervous system disease [3.5%], chronic lung disease 2.5%, chronic kidney disease 1.0%, non-diabetes endocrine diseases 1.0% then tumors 0.5% (23). Regarding the mortality of COVID-19, hypertension is risk

factor of mortality (24) and high risk of dying with odd ratio ( 2.42) and higher risk of developing severe disease or dying from SARS-CoV-2 infection with 2.5-fold (25) in another study 32 of the non-survivors from a group of 52 intensive care unit patients with novel coronavirus disease 2019 (COVID-19 were cerebrovascular diseases (22%) and diabetes (22%) without assessing the treatment (26) All the previous study there was no assessment of antihypertension treatment intake or age of the patients.

### The association of age and COVID-19

Is the association of hypertension with covid-19 anything more than a reflection of the age of hypertensive patients? Because HTN prevalence increases in parallel with aging, this pattern may represent the expected prevalence for the given age group (23) There is lack of data in age group and association with COVID19

Giuseppe Lippi et al meta-regression showed significant odds of COVID-19 severity with hypertension was only seen in those over age 60 years old (25). And in another study the median age of SARS-CoV-2-positive patients who died was 78.5 years (median, 80 years; range, 31-103 years; interquartile range, 73 to 85 years) (23) A retrospective study from three hospitals designated for the treatment of COVID- 19 Jinyintan Hospital in Wuhan, Shanghai Public Health Clinical Center in Shanghai, and Tongling People's Hospital in Anhui Province, China , the critical group that had a higher percentage of patients are aged >75 (27)(Table2).

**Table 2.**

Study	Result
Guan et al. (17)	1099 patients with confirmed COVID-19, of which the single highest risk factor of infection was hypertension reported in 15% of patients
Zhang et al. (18)	140 patients with COVID-19 and found 30% of all patients and 37.9% of those with severe disease had hypertension
Li, B et al. (20)	meta-analysis of six studies. 1527 patients. -hypertension was present in 17.1% of patients with the infection -patients with severe symptoms had a twofold likelihood of being hypertensive compared to non-severe/non-ICU patients
Zhou F et al. (21)	The most common comorbidities in one report were hypertension (30%), diabetes (19%), and coronary heart disease (8%)
Huang et al. (22)	-113 patients with hypertension -Elderly with comorbidities -multivariate analysis (adjusted for age and sex) failed to show that hypertension was an independent risk factor for COVID-19 mortality or severity. -Compared with non-hypertensive patients, hypertensive patients had a higher mortality rate (24.8% vs 15.2)
Wu C et al. (23)	-(32.8%) of the patients had comorbidities. hypertension represent [19.4%] of them - The median age of SARS-CoV-2-positive patients who died was 78.5 years

Morra ME et al. (24)	hypertension increased the risk of mortality
Giuseppe Lippi et al. (25)	- observed that hypertension carries a nearly 2.5-fold higher risk of developing severe disease or dying from SARS-CoV-2 infection h-risk of dying with odd ratio ( 2.42) ic-significant odds of COVID-19 severity associated with tension was only seen in those over age 60
Fang L et al. (26)	32 of the non-survivors ICU COVID19 2019 (were cerebrovascular diseases (22%) and diabetes (22%). (26)
Feng Yet al. (27)	The critical group had a higher percentage of patients aged >75 years than the moderate group

## ACE2 and ARB

SARS-COV-2 enter the cells through angiotensin converting enzyme 2 (ACE2) receptor (6). which is expressed by epithelial cells of the blood vessels, lung, intestine and kidney (25) ACE inhibitors and angiotensin receptor blockers (ARBs) are antihypertensive medication upregulate the ACE2 (26) and increases its expression. Consequently, the increased expression of ACE2 would facilitate infection with COVID-19 (28) by supplying SARS-CoV-2 with a more of "anchors" for infecting cells (25) RAAS activation plays a major pathogenic role in HTN through hemodynamic actions and cytokines and intracellular signaling pathways, which ultimately promote many adverse cellular processes result in systemic damage. (29) Many hypothesis been raising about which is more beneficial or should withdrawing the medication? Although the number of fatal COVID-19-positive patients treated with ACEIs was more than twice the number of those treated with ARBs, it cannot definitely conclude the risks or benefits of these therapies due to confounding variables of age, HTN, and impact of yet-unidentified comorbidities on outcome with the COVID-19 pandemic. (23) ACE2 limits the adverse vasoconstrictor and profibrotic effects of Ang II through its degradation and by counteracting its actions through the formation of Ang 1-7. The high expression of ACE2 in heart, type II alveolar cells, capillary endothelium, and enterocytes demonstrates its essential role in the CV and immune systems, being principally involved in heart function and the development of HTN and complications of diabetes mellitus (DM) Sanchis- Gomar et al study suggest that ARBs might be a better treatment option in COVID-19 patients at higher risk of severe forms of disease due to the equal efficacy but fewer side effects than ACEIs (30-32).

A report of 476 patients with COVID-19 that moderate COVID-19 hypertensive patients are higher usage of ARBs with than those with a severe and critical course of the disease and there are no data regarding the association between RAAS inhibitors and the outcome (33) on other hand Marijana Tadic et al study conclude that no advantage to any group of medications within RAAS inhibitors. (3)and there was no association between ACEI/ARB use and the risk of COVID- 19 (34) and there is no association

with the severity or mortality of COVID-19 patients (20) Regarding Withdrawing these medications or switching therapy would have uncertain benefits, but definitely many disadvantages such as uncontrolled hypertension, cardiac decompensation and renal function impairment, which could potentially induce more complications in patients with COVID-19 than the infection of SARS-CoV-2 itself (34) (Table3).

**Table 3.**

Study	Results
Sanchis-Gomar et al. (30)	suggested that ARBs might be a better treatment option in COVID-19 patients at higher risk of severe forms of disease due to the equal efficacy but fewer side effects than ACEIs
Marijana Tadic et al. (3)	-There is no advantage to any group of medications within RAAS inhibitors. -Withdrawing these medications or switching therapy would have uncertain benefits, but definitely many disadvantages such as uncontrolled hypertension, cardiac decompensation and renal function impairment, which could potentially induce more complications in patients with COVID-19 than the infection of SARS-CoV-2 itself.
Feng et al. (29)	-investigated 476 patients with COVID-19 and reported a significantly higher usage of ARBs in hypertensive patients with moderate COVID-19 disease than those with a severe and critical course of disease - There are no data regarding the association between RAAS inhibitors and the outcome.
Li, B et al. (20)	included 1178 patients with COVID-19, out of which 362 had hypertension and reported that ACEIs/ARBs are not associated with the severity or mortality of COVID-19 patients
Mancia G et a. (34)	there was no association between ACEI/ARB use and the risk of COVID-19

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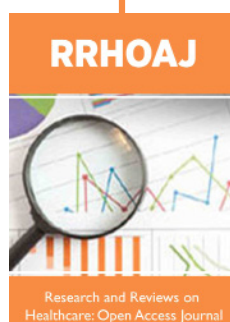
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