






REVIEW

## Covid-19 in patients with Arterial Hypertension

## Covid-19 en pacientes con Hipertensión Arterial

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### ABSTRACT

**Introduction:** high blood pressure is a risk factor for worsening health in patients with COVID-19.

**Objective:** to characterize the treatment of high blood pressure during the COVID-19 pandemic.

**Method:** a descriptive literature review was conducted using data collected between 2019 and 2021 worldwide with the aim of gathering up-to-date information on high blood pressure during Covid-19. We used different search engines and nationally and internationally renowned bibliographic resources, including the SciELO database, the Virtual Health Library, and scientific articles from journals, which were chosen for their up-to-date content on the subject and their accuracy. The research was conducted in accordance with the principles of medical ethics.

**Results:** hypertensive patients are more likely to develop severe cases of COVID-19 compared to healthy individuals. The prescribed medication to control high blood pressure must be followed.

**Conclusions:** the most recent evidence shows that people with untreated high blood pressure appear to be at greater risk of complications associated with COVID-19. Extreme measures should be taken to prevent the spread of infection among these patients, who in turn should lead a healthy lifestyle to keep their defenses strong.

**Keywords:** Hypertension; Covid-19; Risk Factor; Treatment.

### RESUMEN

**Introducción:** la hipertensión arterial constituye un factor de riesgo para el agravamiento del estado de salud de pacientes con Covid-19

**Objetivo:** caracterizar el tratamiento de la hipertensión arterial en tiempos de Covid-19.

**Método:** se realizó una revisión bibliográfica descriptiva con datos recopilados entre el 2019 y el 2021 a nivel mundial con el objetivo de reunir información actualizada sobre hipertensión arterial en tiempos de Covid-19. Utilizamos diferentes buscadores y recursos bibliográficos de prestigio nacional e internacional entre ellos la base de datos de SciELO, Biblioteca Virtual de Salud y artículos científicos de revistas, estos fueron escogidos por su contenido actualizado sobre el tema y su veracidad. Se realizó la investigación con respeto a los principios de la ética médica.

**Resultados:** los pacientes hipertensos son más propensos a presentar cuadros graves de la COVID-19 en comparación con personas sanas. Se debe seguir la medicación indicada para controlar la presión alta.

**Conclusiones:** la evidencia más reciente muestra que las personas con hipertensión arterial no tratada parecen estar a más riesgo de complicaciones asociadas con la COVID-19. Se deben extremar las medidas para evitar

el contagio de estos pacientes, y estos a su vez llevar un estilo de vida saludable que mantenga altas sus defensas.

**Palabras clave:** Hipertensión; Covid-19; Factor de Riesgo; Tratamiento.

## INTRODUCTION

Hypertension is when the blood vessels have persistently high blood pressure, which can damage them. It is a preventable disease or can be postponed through a set of interventions; it can be reduced by consuming less salt and eating a balanced diet, maintaining proper weight, avoiding alcohol consumption, eliminating tobacco and drugs, and exercising regularly.<sup>(1)</sup>

In 2019, on 31 December, in Wuhan City, located in Hubei in the South Central region, authorities reported that 27 people related to a seafood market debuted with acute respiratory syndrome of unknown cause, with seven in serious condition. On 7 January 2020, the Chinese authorities reported that a new coronavirus (2019-nCoV) had been identified as a possible etiology of the illness, and after testing ruled out SARSCoV, MERS-CoV, influenza and avian influenza viruses, adenoviruses, as well as other common viral or bacterial respiratory infections. Similar clinical symptomatology is rapidly being reported in different Asian countries and globally. The World Health Organisation declared a global health emergency on 30 January 2020, and in February 2020, the new virus was SARS-CoV-2. On 11 March 2020, COVID-19 was paraded as a pandemic.<sup>(2)</sup>

As of 26 April 2020, 183 countries had reportedly been affected by COVID-19, with 2 844 712 confirmed cases and 201 315 deaths, for a case fatality of 7,07 % (-0,05).<sup>(3)</sup> As of 8 March 2021, a total of 22 082 983 cases of COVID-19 have been reported in Latin America and the Caribbean. Brazil is the region most affected by this pandemic, with around 11 million confirmed cases.<sup>(4)</sup> According to official sources, by the end of 18 March 2021, 65 149 patients had been diagnosed with the disease in Cuba, with 387 deaths.<sup>(5)</sup>

The spectrum of the disease is broad and includes mild, self-limiting illness to severe and progressive atypical pneumonia, multi-organ failure, and death. Increasing evidence indicates an association between several risk factors and worse prognosis in patients with COVID-19. Recent studies raise questions about the increased susceptibility of these patients, as well as the role of hypertension in the progression and prognosis of patients with COVID-19.<sup>(6)</sup>

A meta-analysis including eight studies with 46 248 patients estimated that while the prevalence of hypertension among COVID-19-infected patients is similar to that of the general population, it would appear that this risk factor does not increase susceptibility to infection, having hypertension is associated with more than a two-fold increased risk of developing severe forms of COVID-19.<sup>(7)</sup>

On 6 April 2020, JAMA published data from 1 591 intensive care patients in Lombardy, Italy. High blood pressure (49 %) and cardiovascular disease (21 %) were the most frequent comorbidities, more than cancer (8 %) and chronic obstructive pulmonary disease (4 %). The study stratified the cohort by the presence or absence of hypertension, and those with hypertension had higher mortality (65 % vs 40 %).<sup>(8)</sup> Research in China showed that male patients of advanced age or with associated diseases (or both), including hypertension, with high ACE2 (angiotensin-converting enzyme 2) expression had a worse prognosis during COVID-19.<sup>(9)</sup> In Peru, a meta-analysis of 12 studies found that 35,5 % of patients with hypertension had severe disease.<sup>(6)</sup>

According to the Third National Survey of Risk Factors, 30,9 percent of Cubans over 15 years of age suffer from HTN, which means that 2,6 million people in the country are hypertensive, and this figure could be higher. In the case of children, approximately one to three percent of those over the age of six suffer from it, generally caused by obesity due to poor nutritional habits and little physical activity. Furthermore, from the age of 50 onwards, the risk of hypertension multiplies, and by the age of 60, almost 60 percent of the population suffers from it.<sup>(10)</sup>

In Cuba, arterial hypertension (AHT) is the most frequent comorbidity linked to mortality from the virus. An analysis of all confirmed patients with the new coronavirus in the country, aged 18 years or older, diagnosed between 11 March 2020 - when the first cases were detected in the country - and 15 October of that year showed that more than 47 percent of those who died had AHT. Dr Jorge Luis León Álvarez, one of the researchers, pointed out that these data align with those reported in the rest of the world.<sup>(10)</sup> Hypertension is present in 25,3 percent of Villaclareños over the age of 14.<sup>(11)</sup>

Hypertension is a severe condition that can have serious consequences. A person with this condition should monitor their blood pressure levels frequently. Be vigilant for signs of high blood pressure and maintain a healthy lifestyle.<sup>(12)</sup> Uncontrolled or uncontrolled hypertension causes almost 5 million deaths annually from heart attacks and 2 million deaths from stroke.<sup>(13)</sup> It is a prevalent cardiovascular risk factor in older adults. Similar to what is happening with the coronavirus, it has a more malignant impact on the adult population; therefore, it is one of the most frequent cardiovascular risk factors in infected patients.<sup>(9)</sup>

The research team was motivated to write this article because it is important to know how to treat AHT in the aftermath of COVID-19, especially the pharmacological treatment received by infected patients.

Aim: to characterize the treatment of hypertension in times of Covid-19.

## METHOD

We conducted a descriptive literature review with data collected between 2019 and 2021 worldwide to gather up-to-date information on arterial hypertension during COVID-19. We used different search engines and bibliographic resources of national and international prestige, among them the SciELO database, Virtual Health Library, and scientific articles from journals; these were chosen for their updated content on the subject and their validity. The research was conducted concerning the principles of medical ethics.

## DEVELOPMENT

Blood pressure consists of the force of the blood pushing against the walls of the arteries. When this pressure is very high, it is called arterial hypertension. It forces the heart to work far beyond its capacity, which can damage the blood vessels and can be fatal, as it can lead to a heart attack, cerebrovascular infarction, heart or kidney failure, or visual impairment, among others. As a chronic disease, it is therefore essential to constantly be monitored by the treating physician and not to stop taking the prescribed medication or change doses.<sup>(14)</sup> AHT sometimes, but not always, causes a headache, shortness of breath, dizziness, chest pain, heart palpitations, and nosebleeds. Most people with hypertension do not show any symptoms until they have an associated pathology, which is why it is known as the ‘silent killer’.<sup>(15)</sup>

Fever, cough, dyspnoea, and fatigue are often the initial clinical picture. Other symptoms, such as headache, gastrointestinal, and upper respiratory symptoms (rhinorrhoea and sore throat), are less common. Some patients have smell and taste disorders. Severe COVID-19 results in acute respiratory distress syndrome (ARDS), respiratory failure, arrhythmias, acute cardiac injury, shock, multi-organ failure, and death.<sup>(16)</sup>

The most recent evidence shows that people with untreated high blood pressure appear to be at greater risk of complications associated with COVID-19 than those whose high blood pressure is controlled with medication.<sup>(17)</sup> The older a hypertensive person gets, the more common it is for other concurrent conditions to appear, such as heart problems, diabetes, lung and kidney disease, immunosuppressed states (‘lowered defenses’), etc. These situations and ages over 60-65 determine a higher risk of severe forms of the condition.<sup>(18)</sup>

García Céspedes M. *et al.*<sup>(9)</sup> states, ‘People who present COVID-19 and suffer from other diseases have a higher probability of complications. Similarly, Salazar M *et al.*<sup>(8)</sup> warn that: ‘Patients over 60 years of age, as well as those with cardiovascular disease, should especially avoid exposure to SARS-CoV-2, not self-medicate and consult promptly’.

The research team believes that it is worth considering that hypertension is a clinical predictor of severity in those affected by COVID-19, which is most evident in those over 60 years of age.

When analyzing the essential elements related to the pathophysiology of arterial hypertension, it is particularly significant that this clinical entity is associated with inflammatory factors and that its development could occur through endothelial dysfunction, which is fundamentally characterized by an imbalance in the production of substances with vasoconstrictor and vasodilator actions, predominantly the former, leading to a state of hemodynamic dysfunction of varying intensity, or by activation of the renin-angiotensin system, which has also been associated with vascular inflammation, with deleterious effects on the immune system, which conditions the appearance of complications, especially if infection by the SARS-CoV-2 virus is contracted.<sup>(9,17)</sup>

The renin-angiotensin-aldosterone system is present in hypertensive patients, as in patients with other cardiovascular and renal diseases. This system comprises peptides and enzymes that lead to the synthesis of angiotensin II, the effects of which are mediated by the action of AT1 and AT2 receptors and are involved in the control of cardiovascular function and hemodynamic balance.<sup>(9)</sup>

The multiple interactions between SARS-CoV-2 and the renin-angiotensin-aldosterone system (RAAS) have generated significant interest and editorials in high-impact journals and concerns in the medical community.<sup>(8)</sup> The coronavirus binds to target cells via angiotensin-converting enzyme 2 (ACE 2), which is expressed in epithelial cells of the lung, intestine, kidney, and vessels. ACE2 expression increases in people with chronic disease, particularly those treated with ACE inhibitors (ACE inhibitors) or angiotensin II type 1 receptor antagonists (ARBs).<sup>(16)</sup>

The fundamental action of ACE inhibitors is to inhibit the conversion of the enzyme angiotensin I to angiotensin II, thereby limiting the vasoconstrictor effect of this enzyme at the peripheral level. ACE inhibitors are excellent antihypertensive agents in single doses or combined with other antihypertensives, mainly diuretics. Their beneficial effect in reducing cardiovascular morbidity and mortality in both hypertensive diabetic and non-diabetic patients has been proven.<sup>(20)</sup> They are attributed with beneficial actions on vascular remodeling in the heart and blood vessels and a nephroprotective effect by reducing proteinuria. They also have other advantages, such as a neutral lipid profile, improved insulin sensitivity, and do not cause hyperuricemia. They

are the drugs of choice in patients with hypertension and diabetes mellitus and even in non-hypertensive diabetics due to their effective nephroprotection, as mentioned above. The most commonly used ACE inhibitors are enalapril, captopril, lisinopril, ramipril, perindopril, and fosinopril, all with one or at most two doses per day and proven hypotensive action.<sup>(9)</sup>

Angiotensin II receptor antagonists exert vasodilatory action by blocking the enzyme angiotensin II at its AT1 receptors. Their antihypertensive actions are similar to those of ACE inhibitors. Still, they do not have the side effects of ACE inhibitors (cough and angioedema) as they do not potentiate the action of bradykinin. They should be indicated mainly when there is intolerance to ACE inhibitors and especially if there is target organ damage, a history of acute myocardial infarction, heart failure, proteinuria, or left ventricular dysfunction, or in associated clinical conditions, such as metabolic syndrome and type 1 or 2 diabetes mellitus. Numerous products from this drug group are currently on the market, including valsartan, losartan, irbesartan, candesartan, and telmisartan, with varying dosages. Still, their antihypertensive effect is long-lasting and allows for a single daily dose.<sup>(9)</sup>

According to Salazara M et al.<sup>(8)</sup>: “SARS-CoV-2 requires ACE2 to enter the cell, which may favor high levels of infection. Conversely, ACE2 depletion, as observed with age in diabetes and cardiovascular disease, allows overexpression of angiotensin 2-dependent inflammatory mechanisms, which may favor severe forms of infection. ACE2 is widely expressed in type II pneumocytes, heart, and blood vessels, which may explain the predilection of the virus for the lung and cardiovascular system. Converting enzyme inhibitors (ACE inhibitors) and angiotensin two receptor blockers (ARBs) can increase ACE2 levels and, as a result, could potentially both promote infection and protect against the development of severe forms.” However, Cando Herrera J et al.<sup>(17)</sup> states that: ‘abrupt discontinuation of ACEI and ARA II therapy may lead to clinical instability and unfavorable outcomes in these patients.’

Discontinuation of medication will likely lead to loss of control of blood pressure figures, and this situation, in turn, predisposes the person to cardiac complications, strokes, etc. Therefore, the recommendation is not to stop taking the remedies. There is no evidence that it is necessary to change an antihypertensive treatment unless expressly instructed to do so by your doctor.<sup>(18)</sup>

OSPAT<sup>(13)</sup> states that: ‘Although it was said early in the epidemic that drugs in the ‘pril’ family (angiotensin 2-converting enzyme inhibitors, such as enalapril) and “sartans” (angiotensin receptor blockers, such as losartan) could be dangerous in people with COVID-19, experts say they are safe and effective for both patients with hypertension and heart failure’.

The research team believes that until there is more conclusive research on whether medication to control hypertension helps the severity of COVID-19, it should be held off.

The scientists found that antihypertensive drugs can also influence how quickly the immune system can reduce the viral load - the virus concentration in the body. Here, there is a clear difference between the different forms of treatment for hypertension - in patients treated with angiotensin II receptor blockers, the reduction in viral load was significantly delayed, which could also contribute to a more severe course of COVID-19, he explained, such a delay is not observed in patients receiving ACE inhibitors to treat their hypertension.<sup>(20)</sup>

The research team believes that treating hypertension with ACE inhibitors may be more beneficial for patients with COVID-19 than treating it with angiotensin II receptor blockers. This hypothesis is currently being further investigated in randomized trials.

Recommendations for patients with hypertension in the context of the COVID-19 pandemic include:<sup>(21)</sup>

- Do not abandon the medication prescribed by your primary care team. Continuing as usual with their chronic medication is very important to avoid decompensation of their baseline situation.
- Maintain the best possible lifestyle. It isn't easy to maintain, but trying to lead the best possible lifestyle is very important, as is eating a low-salt, low-fat diet rich in vegetables, skimmed dairy products, and legumes. Avoid convenience foods. Avoid a sedentary lifestyle; regular exercise increases life expectancy. Try to do a minimum amount of exercise, for example, at home, no matter how small the house is. The benefit of exercise is no excuse for going out shopping every day. Confinement is essential. Find a place in the house to exercise, and exercise in a way that is comfortable for you, according to your condition.
- Continue to measure your blood pressure as you have been doing.

## CONCLUSIONS

When blood pressure is very high, it is referred to as high blood pressure, which forces the heart to work well beyond its capacity. The latest evidence shows that people with untreated high blood pressure appear to be at higher risk of complications associated with COVID-19 than those who are controlled with medication. Experts say that drugs for this disease are safe and effective and do not represent a favourable component for the aggravation of patients with hypertension. Extreme measures should be taken to avoid infecting these patients, and they, in turn, should lead a healthy lifestyle that keeps their defenses up.



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