

# Arterial Hypertension and Diabetes Mellitus as Risk Factors in the Evolution of Patients with COVID-19

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**Abstract:** COVID-19 is one of the most relevant pathologies in recent months, becoming one of the most deadly pandemics that the world has faced; Since the detection of the first cases in Wuhan (China) until today, the evolution of those infected has been a bit unpredictable, although without a doubt comorbidities such as Diabetes Mellitus (DM) and Arterial Hypertension (HTN) have been an essential link in fatality of clinical evolutions and the main cause of transfer to intensive care units. A bibliographic analysis was carried out, using the Scielo, Scopus, EBSCO and Google Academic databases, where information was obtained from twenty-two bibliographic references in order to determine the influence of arterial hypertension and diabetes as risk factors in the evolution of patients with covid 19. Patients diagnosed with COVID-19 who have hypertension and diabetes as a personal medical history are more likely to develop complications during the course of the disease and even die. The control and isolation of these patients is of special importance, taking into account the risk posed by presenting these pathologies. The research work carried out in Cuba maintains the control and knowledge of the health personnel of the state of vulnerable patients.

**Keywords:** Diabetes Mellitus, Arterial Hypertension, COVID-19

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## 1. Introduction

Respiratory viral infections continue to emerge as a challenge for public health, some of the examples in the last two decades are the SARS-Cov (Severe Acute Respiratory Syndrome coronavirus) in 2002, in 2009 the H1N1 influenza and in 2012 the MERS- CoV (Middle East Respiratory Syndrome coronavirus). Last December 2019, the third new coronavirus emerged in the last 17 years, specifically in Wuhan Hubei province, China; named SARSCoV-2 (severe acute respiratory syndrome coronavirus 2) responsible for the disease named in February 2020 as COVID-19 by the World Health Organization (WHO).[1]

The recent global COVID-19 emergency caused by SARS-CoV-2 was declared a pandemic by the World Health

Organization (WHO) on March 11, 2020. COVID19 is a severe acute respiratory syndrome caused by a new Coronavirus identified in the city of Wuhan, capital of Hubei province in China, in December 2019. The clinical manifestations of COVID-19 vary from an asymptomatic disease, to a severe condition with respiratory failure, multi-organ dysfunction, septic shock and death. The most common symptoms are fever, dry cough, and fatigue. However, some COVID-19 patients develop vomiting, diarrhea, and abdominal pain during the course of their illness. [2]

The appearance of epidemics is not something new in the history of humanity, but in recent years, we are witnessing epidemic outbreaks, many of them due to viruses, which cause social alarm. [3]

The reasons why these outbreaks have more impact are human reasons and derive from our way of life (living in big

cities, more trips for leisure or business, commercial exchanges) and from the hyper information that exists where the mass media, formal or informal, they keep us updated minute by minute of the development of any event of global impact. [3]

This disease is spreading in Latin America, reporting its first cases at the end of February in Brazil, Mexico and Ecuador, and in April 201,977 cases were reported in this region. [4]

On March 11, 2020, the first three imported cases of the disease from Italy, detected in the municipality of Trinidad, in the Sancti Spiritus province, are notified in Cuba. [4]

As of February 21, 2021, 111,747,462 cases and a fatality of 2.21 have been reported in the world. Latin America, in turn, reports 50,263,114 cases (+183,516), representing 44.97% of the world's cases and a fatality of 2.36. Cuba, thanks to the measures taken by the national health system, maintains extremely low figures compared to other countries, 839 new cases were reported this day, for a total of 45,361 cases, only 1.98% of the patients studied by PCR (2 281 712 samples) [5]

What is the influence of hypertensive and diabetic antecedents in the evolution of positive patients for covid 19?

Objective: To determine the influence of high blood pressure and diabetes as risk factors in the evolution of patients with covid 19.

## 2. Development

Coronaviruses (CoVs) are a group of viruses that cause illnesses ranging from the common cold to serious infections. There are four main subgroups: alpha, beta, gamma, and delta.

Common human coronaviruses:

- 1) 229E (alpha coronavirus)
- 2) NL63 (alpha coronavirus)
- 3) OC43 (beta coronavirus)
- 4) HKU1 (beta coronavirus)

Other human coronaviruses:

MERS-CoV (the beta coronavirus that causes Middle East Respiratory Syndrome, or MERS) [1]

According to the evidence available to date, the virus spreads mainly from person to person through close contact, even among health workers who care for patients with COVID-19, which would be consistent with what is known on other similar pathogens such as SARS and MERS-CoV.

Transmission can be direct by small droplets (gout transmission) that occur when a person coughs or sneezes. These droplets can reach the mouth or nose of people who are less than 1.8 meters, mainly 1 meter, who can inhale them when breathing.

An indirect form of transmission occurs when these droplets remain on objects or surfaces and the individual touches them and then touches their eyes, mouth or nose with contaminated hands (contact transmission). Studies have been carried out with taking environmental samples in the rooms of patients with COVID 19 and it was observed that the contamination occurs mainly on the surfaces closest to the patients and no particles suspended in the air were

detected. This means in principle that COVID 19 is not transmitted through the air, but through droplets. [6]

### 2.1. Arterial Hypertension

Nowadays, arterial hypertension (HTN) is one of the most common diseases that affect human health, being an important pathology and risk factor for other diseases. [7]

(HT) is a chronic disease in which the pressure with which the heart pumps blood to the arteries increases, so that it circulates throughout the body. [8]

Hypertension is considered a disease of multifactorial origin, among them heredity, environmental, hemodynamic and humoral factors. The role of atrial natriuretic peptide, a substance related to changes in atrial pressure and hypotension, neuropeptide G, which behaves as a co-transmitter of norepinephrine and can participate in the physiological control of vascular tone and release in situations of stress. Active substances such as prostacyclin, nitric oxide or factor derived from the endothelium with vasodilator actions and a peptide with great vasoconstrictor action are produced in the vascular endothelium; they intervene directly or by interaction with other cells on vascular tone. [7]

SARS-CoV-2 enters the cell using as receptor the angiotensin converting enzyme 2 (ACE2), a membrane exopeptidase present mainly in the epithelium of the airway, lung parenchyma, vascular endothelium, brain, kidney, heart, testicular tissue and intestine. Therefore, patients with SARS-CoV-2 may have multisystem involvement. [9]

The foregoing generated great expectations regarding the potential risk of using two groups of antihypertensive drugs in patients with COVID-19. These groups of antihypertensive drugs are the angiotensin converting enzyme (I-ACE) inhibitors and the angiotensin II AT1 receptor antagonists (ARBs), which have been used for decades in the treatment of hypertension and heart failure. and both with strong evidence on the benefit in cardiovascular morbidity and mortality in these patients. [10]

Angiotensin converting enzyme (I-ACE) inhibitors and angiotensin receptor blockers (ARA II) may overexpress ACE 2, leading to the hypothesis that this effect may be increased.

In the study by Li et al., Published in JAMA Cardiology, no association was found in patients with hypertension and hospitalized for COVID-19, between the use of I-RCT / AIIIRA with severity or mortality from COVID-19 in this group of patients. [10]

Mehra et al. Found similar results to previous studies, without finding a potential deleterious association of the use of I-RCT or ARA II with in-hospital mortality and the use of I-RCT / AIIIRA. Mancina et al. In Lombardy, Italy, report a study of 6,272 cases and 30,759 controls, in which no evidence was found that the use of I-RCT or ARA II affected the risk of COVID-19. [10]

The evidence available at the moment suggests that people with chronic non-communicable diseases (NCDs) are at greater risk of serious complications (hospitalization in intensive care, need for use of mechanical ventilation and

death) from COVID-19 infection. [11]

It has been reported that the severity of the clinical presentation of COVID-19 depends on several genetic factors (polymorphisms in the ACE2 and TMPRSS2 genes and non-genetic ones (advanced age, male gender, and presence of comorbidities). In particular, several investigations have contributed evidence of association between severe forms of COVID-19 and the presence of a personal pathological history of hypertension, diabetes mellitus, or chronic kidney disease. [12]

A retrospective study carried out in Wuhan, showed that the patients who did not survive had a mean age of 69 years and hypertension was the most frequent comorbidity with 48% followed by diabetes with 31% and ischemic heart disease with 24%. In Italy, the Italian Health Institute reported in March that in 2003 patients with a mean age of 79.5 and a mean of 2.7 comorbidities per patient, as in China, arterial hypertension was the most prevalent comorbidity with 76.1%, followed by diabetes mellitus with 35.5% and ischemic heart disease with 33.3%. The high prevalence of hypertension among older adults is a recognized fact. [13]

Patients with any form of heart disease can have a 10.7% mortality rate in COVID-19 and hypertension of 6%. [13]

The presence of comorbidities in severe cases of COVID-19 has been widely demonstrated. Data from the onset of the pandemic in China show that, while mortality without comorbidities was 0.9%, it increased to 10.5% with cardiovascular disease, 7.5% with diabetes, and 6.3% with obstructive pulmonary disease chronic, 6% with arterial hypertension and 5.6% with cancer. In an analysis of 1,590 patients admitted to different cities in China, the presence of a comorbidity increased the risk of a combined end point of ICU admission, MRA, or death (adjusted for age) by ~ 80% (HR 1.79, 95% CI 1.16 -2.77) and the presence of two or more comorbidities in more than 2 times (2.59, 95% CI 1.61-4.17). The most common risk factors were high blood pressure and diabetes, both of which increased the risk by ~ 60%. A meta-analysis, also from China, which included 8 studies with 46,248 patients estimated that patients with arterial hypertension had > 2 times the risk of suffering from severe forms of COVID-19 and those with cardiovascular disease more than three. In the Lombardy cohort of severe cases admitted to ICU, arterial hypertension (49%), cardiovascular diseases (21%) and diabetes (17%) were the most frequent comorbidities, more than cancer (8%) and that chronic obstructive pulmonary disease (4%). The study stratified the cohort by the presence or absence of hypertension and hypertensive patients had higher mortality (65% vs 40%,  $p < 0.001$ ). However, this data should be taken with caution since 58% of the patients were still hospitalized at the time of the analysis, in addition to the fact that the hypertensive patients were older. Also in Italy, the analysis of a group of 355 deceased patients in whom a detailed clinical history was available, confirms the association of mortality with cardiovascular diseases and diabetes; 30% had coronary artery disease, 24.5% atrial fibrillation, 9.6% had a history of stroke, and 39.5% were diabetic. Only 3 patients (0.8%) had no underlying disease and  $\frac{3}{4}$  parts had 2 or more

comorbidities. In the cohort of cases hospitalized in New York, arterial hypertension (56%), obesity (41.7%) and diabetes (33.8%) were the most frequent comorbidities. [14]

80.8% of those who died in Colombia had some comorbidity, similar to what has happened in other countries. This confirms that COVID-19 affects more people with an adverse health history. Of the total deaths up to May 7, 2020 in Colombia, 4 out of 10 people suffered from arterial hypertension. Reviewing the publication by Zhou et al, from Wuhan (China), we found a retrospective cohort in which 191 patients were included, of which up to 48% had comorbidities, hypertension being the most common (58 patients, 30%) [15]

To date, there is no treatment or specific effective vaccine for COVID-19, with prevention being the most important measure. [11]

## 2.2. Mellitus Diabetes

Diabetes mellitus is a syndrome characterized by generalized metabolic disorders in which the dominant factor is chronic hyperglycemia. Inadequate glycemic control favors the development of acute and chronic complications, increases the risk of disability and affects the quality of life of patients. [16]

Between 3% and 4% of the world's population is sick with diabetes, a condition that occurs when the pancreas cannot make enough insulin or when it fails to act in the body, because the cells do not respond to its stimulus, which leads to a significant risk towards other diseases, thus reducing the quality of life by an average of 10 or more years. According to the World Health Organization (2018), 70% of people with diabetes live in low- and middle-income countries; in Mexico approximately 425, 345 inhabitants suffer from diabetes. [17]

In general, people with diabetes face higher risks of complications when it comes to viral infections such as influenza, flu, and that is likely to apply to COVID-19 as well. [18]

The severity of the clinical presentation of COVID-19 has been reported to depend on several genetic factors (polymorphisms in the ACE2 and TMPRSS2 genes) and non-genetic factors (advanced age, male gender, and the presence of comorbidities). In particular, several investigations have provided evidence of association between severe forms of COVID-19 and the presence of a personal pathological history of hypertension, diabetes mellitus or chronic kidney disease. The identification of comorbidities associated with the severe clinical presentation of COVID-19 is important for the appropriate therapeutic approach to affected patients, and for the development of health strategies aimed at the prevention and treatment of medical complications in the context of this disease. Based on the evaluation of 13 studies, an overall risk of 3.53 was obtained. (95% CI: 2.79-4.47;  $p < 0.001$ ) of suffering from COVID-19 with severe presentation, in patients with diabetes mellitus. [12]

In the United States, within the population over 64 years of age, considered the highest risk for dying from COVID-19, almost 27% have diabetes mellitus. Another study

carried out in patients with diabetes mellitus and COVID-19 showed that 69% had elevated capillary glucose monitoring values and 10% had at least one episode of hypoglycemia. On the other hand, it has been postulated that pancreatic tissue could be affected by viral infection, with the consequent alteration of hydrocarbon metabolism. Last but not least, the anxiety state described in patients with SARS-Cov-2 infection in the patient with diabetes could worsen hyperglycemia. Patients with diabetes usually have other comorbidities such as hypertension, chronic obstructive pulmonary disease, coronary heart disease, cerebrovascular disease, chronic kidney disease, which makes them an extremely vulnerable population to present a severe disease due to COVID 19 and a high risk of hospitalization in ICU and death. [19]

The effects of COVID-19 on the endocrine system are not yet well established; however, individuals with diabetes mellitus (DM) who suffer from COVID-19 have a higher fatality rate (between 10% and 11%), which establishes that DM is a risk factor for fatal outcomes among those who suffer from COVID-19. [20]

There are several hypotheses that could explain why these patients have a higher incidence and severity. It is well known that the person with DM2, per se, has a greater risk of infection, mainly due to a defect in innate immunity that affects phagocytosis, neutrophil chemotaxis and cellular immunity, which makes them especially vulnerable. It is also true that the high frequency of DM2, in severe cases of COVID-19, could simply reflect the higher prevalence of DM2 in the elderly, in addition to the fact that these patients also have more comorbidities, including cardiovascular disease. Therefore, despite the fact that respiratory symptoms are predominant in COVID-19 infection, DM2 takes on a special interest in this disease: both the risk of virus infection and its severity increase in these patients. [21]

The next question that arises is what mechanisms could connect COVID-19 infection with endocrine system disruption. The virus enters the cell using angiotensin converting enzyme 2 (ACE2) as a receptor, a membrane exopeptidase present mainly in the kidney, lungs and heart, but also in other organs, such as endothelial cells and the pancreas. [21]

Cardiovascular disease and diabetes are the most frequent comorbidities among those hospitalized. Fatality According to the series published by the Chinese CDC, with a total of 1,023 deaths among confirmed cases (44,672), the crude fatality was 2.3%. Patients who did not present comorbidities had a lower case fatality rate (around 0.9%), compared to patients with comorbidities who had much higher rates (10.5%). [22]

### 3. Conclusions

According to what has been reviewed, arterial hypertension and diabetes mellitus are the main pathologies that cause aggravation of patients diagnosed with covid 19. These diseases are the first causes of transfer to intensive care units. Cuba carries out continuous research work in

which it has identified its vulnerable patients by health zones, maintaining their protection.

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