ORIGINAL ARTICLE

INVESTIGACIÓN en DISCAPACIDAD

Vol. 8, No. 3
September-December 2022
pp 85-90

doi: 10.35366/107508

# Complicity of the pre-existing clinical phenotype with the outcome of death in COVID-19 patients

## *Complicidad del fenotipo clínico preexistente con el resultado de muerte en los pacientes de COVID-19*

Laura E Martínez-Gómez,[1] Brígida Herrera-López,[1]
Carlos Martinez-Armenta,[2] Silvestre Ortega-Peña,[1]
Dafne L Guido-Gómora,[3] María Carmen Camacho-Rea,[4]
Carlos Suárez-Ahedo,[1] Paola Vázquez-Cárdenas,[5] Gilberto Vargas-Alarcón,[6]
Gustavo Rojas-Velasco,[6] José Manuel Fragoso,[6] Rosa P Vidal-Vázquez,[5]
Juan P Ramírez-Hinojosa,[5] Felipe de J Martínez-Ruiz,[7]
Dulce M Zayago-Ángeles,[7] Mónica Maribel Mata-Miranda,[8]
Gustavo Jesús Vázquez-Zapién,[8] Adriana Martínez-Cuatzitl,[8]
Edith Barajas-Galicia,[9] José Manuel Rodríguez-Pérez,[6]
Roberto Coronado-Zarco,[1] Vania Lucas-Tenorio,[1] Rafael Franco-Cendejas,[1]
Luis Esaú López-Jácome,[1] Rocío Carmen Vázquez-Juárez,[1]
Jonathan J Magaña,[1] Julio Granados,[4] Luis Rámos-Tavera,[4] Carlos Pineda,[1]
Gabriela Angélica Martínez-Nava,[1] Alberto López-Reyes[1]

**Keywords:**
COVID-19, epidemiology, factors risk.

***Palabras clave:***
*COVID-19, epidemiología, factores de riesgo.*

[1] Laboratorio de Gerociencias, Dirección General, Medicina de Rehabilitación, Laboratorio de Infectología, Departamento de Reconstrucción Articular, Laboratorio de Medicina Genómica, Laboratorio Facilitador. Instituto Nacional de Rehabilitación «Luis Guillermo Ibarra Ibarra», Secretaría de Salud, Ciudad de México, México.
[2] Postgrado en Biología Experimental, Dirección de Ciencias Biológicas

## ABSTRACT

**Introduction:** The Coronavirus Disease (COVID-19) has been a public health problem worldwide for a considerable time. According to the COVID-19 dashboard at Johns Hopkins University (JHU), Mexico is in the fourteenth place of reported cases. Some studies have described some risk factors associated with having COVID-19. However, the risk to develop different COVID-19 outcomes is unclear. **Objective:** To describe the risk factors for develop different COVID-19 outcomes. **Material and methods:** We carried out a multicenter cross-sectional study, from June 2020 to March2021. A non-probabilistic sampling study design was used. For continuous variables Kruskal-Wallis test was carried out for comparing nonparametric distribution among studied groups. $\chi^2$ test was performed for the categorical variables. Univariated logistic analysis was performed to determine the associations of risk factors to COVID-19 outcomes. The analysis was performed using the STATA v.13 software. **Results:** We analyzed 713 patients and were classified as mild (N = 193, 27%); severe (N = 232, 32%); critical (N =169, 24%) and deceased (N = 119, 17%). Critical and deceased group had a highest percentage of males with 121 (72%) and 75 (63%) respectively. The main comorbidities were overweight (N = 221, 31%), obesity (N = 215, 30%) and type 2 diabetes (N = 208, 29%). Others comorbidities were smoking (17%), cardiopathies (3%), alcoholism (2%) neumopathies (1.6%) and nefropahties (1.5%). **Conclusion:** The main risk factors in deceased group were overweight and type 2 diabetes.



**How to cite:** Martínez-Gómez LE, Herrera-López B, Martinez-Armenta C, Ortega-Peña S, Guido-Gómora DL, Camacho-Rea MC et al. Complicity of the pre-existing clinical phenotype with the outcome of death in COVID-19 patients. Invest Discapacidad. 2022; 8 (3): 85-90. https://dx.doi.org/10.35366/107508

y de la Salud (DCBS), Universidad Autónoma Metropolitana Iztapalapa, Ciudad de México, México.
[3] Facultad de Estudios Superiores Iztacala, Universidad Nacional Autónoma de México, México.
[4] Departamento de Nutrición Animal, Departamento de Inmunogenética, Instituto Nacional de Ciencias Médicas y Nutrición «Salvador Zubirán», Secretaría de Salud. Ciudad de México, México.
[5] Centro de Innovación Médica Aplicada, Hospital General «Dr. Manuel Gea González», Ciudad de México, México.
[6] Departamento de Biología Molecular, Instituto Nacional de Cardiología «Ignacio Chávez», Ciudad de México, México.
[7] Nuevo Hospital General Delegación Regional Sur de la Ciudad de México, ISSSTE.
[8] Laboratorio de Biología Celular y Tisular, Laboratorio de Embriología, Escuela Médico Militar, Universidad del Ejército y Fuerza Aérea, Ciudad de México, México.
[9] Servicio de Cirugía General, Hospital Central Norte Petróleos Mexicanos (PEMEX), Estado de México, México.

*Correspondence:*
**Alberto López-Reyes**
**E-mail:** allorey@yahoo.com

**Gabriela Angélica Martínez-Nava**
**E-mail:** ameria.justice@gmail.com

*Received: June 7, 2022*
*Accepted: August 17, 2022*

***RESUMEN***

***Introducción:*** *La COVID-19 se ha convertido en un problema de salud pública a nivel mundial. De acuerdo al COVID-19 dashboard de la Universidad de Johns Hopkins (JHU), México ocupa el catorceavo lugar de casos reportados a nivel mundial. Algunos estudios han descrito factores de riesgo para contraer COVID-19. Sin embargo, los factores de riesgo para desarrollar los distintos desenlaces de COVID-19 no han sido identificados con claridad.* ***Objetivo:*** *Describir los factores de riesgo para desarrollar diferentes desenlaces de COVID-19.* ***Material y métodos:*** *Se llevó a cabo un estudio transversal multicéntrico durante junio del 2020 a marzo del 2021. Se utilizó un muestreo no probabilístico. Para las variables continuas no paramétricas se utilizó la prueba de Kruskal-Wallis. Para variables categóricas se utilizó $\chi^2$. Se realizó regresión logística univariada para determinar las asociaciones de los factores de riesgo para COVID-19. El análisis se realizó en STATA 13.* ***Resultados:*** *Se analizaron 713 pacientes que fueron clasificados como: moderado (N = 193, 27%); severo (N = 232, 32%); críticos (N = 169, 24%) y fallecido (N = 119, 17%). En los grupos crítico y muerto predominó el género masculino con 121 individuos (72%) y 75 (63%), respectivamente. Las principales comorbilidades fueron sobrepeso (N = 221, 31%), obesidad (N = 215, 30%) y diabetes tipo 2 (N = 208, 29%). Otras comorbilidades en la población total fueron tabaquismo (17%), cardiopatías (3%), alcoholismo (2%), neumopatías (1.6%) y nefropatías (1.5%).* ***Conclusiones:*** *Los principales factores de riesgo en el grupo de fallecidos fueron sobrepeso y diabetes tipo 2.*

## INTRODUCTION

In 2019 began the COVID-19 pandemic, the first reports of cases were in Wu Han China and rapidly was transmitted to other countries.[1] SARS-CoV-2 infection is responsible of COVID-19,[2] this virus promotes mainly pneumonia. To date, there are 586,632,358 cases confirmed and 6,424,508 deaths have been attributed to COVID-19. In Mexico, 6,859,970 cases have been confirmed and 328,342 deaths have occurred.[3]

The SARS-CoV-2 has a genome size of approximate 29,891bp and contains a positive-sense single stranded RNA genome packed in the envelope protein.[4] The SARS-CoV-2 replicate primarily in the epithelial cells of the lower respiratory tract and can extended to cells of the upper respiratory tract. The mechanism of transmission began mainly from patients with recognized disease.[5] The transmission of SARS-CoV-2 include direct contact with the aerial droplets released during the conversation, coughing, and sneezing by infected persons. The most common symptoms of COVID-19 are fever, fatigue, dry cough, dyspnea, and malaise. Less common symptoms are sputum production, headache, diarrhea, sore throat, chest pain, nausea, and vomiting.[6]

In Mexico the mainly comorbidities that have been described as associated with worst disease progression and death are male gender, age older than 60 years, and cardiometabolic comorbidities.[7]

The aim of the present work was to describe the characteristics and clinics and anthropometrics of COVID-19 patients.

## MATERIAL AND METHODS



We carried out a multicenter cross-sectional study. From June 2020 to March2021, patients were recruited from the following public hospitals of the Mexican Governmental Health System: *Instituto Nacional de Rehabilitación «Luis Guillermo Ibarra Ibarra», Instituto Nacional de Cardiología «Ignacio Chávez», Hospital Central Militar, Instituto Nacional de Ciencias Médicas and Nutrición «Salvador Zubirán», Hospital General «Dr. Manuel Gea González», Hospital General ISSSTE «Tláhuac», and Hospital Central Norte Pemex.* The bio-

ethics and research committees of the participating institutions approved this study. Written informed consent was obtained from each participant and the privacy of patient data was stated at the informed consent. This study was conducted following good clinical practices and the Declaration of Helsinki.

## STUDY POPULATION

A non-probabilistic sampling study design was used, as patients were recruited directly from the COVID-19 triage facilities of the participant institutions. Inclusion criteria were not familiarly related, independent of gender, age ≥ 18 years, non-vaccinated with clinical manifestations of COVID-19 and positive RT-PCR test. Exclusion criteria were pregnant women, and incomplete clinical history.

The participants were classified according to Gandhi et al. criteria[8] as follows: mild (N = 193), ambulatory subjects with symptoms such as fever, headache, fatigue, odynophagia, cough, rhinorrhea, diarrhea, anosmia, or dysgeusia, with or without dyspnea or pneumonia, not requiring hospitalization; severe (N = 232), hospitalized individuals with any of the following symptoms: tachypnea (respiratory rate > 30 bpm); pulmonary infiltrate > 50%, dyspnea after small efforts; and critical (N = 169), patients requiring invasive mechanical ventilation who could course to shock and multi-organ failure; and those who died (N = 119 individuals).

## STATISTICAL ANALYSIS

The normality of the variables distribution was evaluated. For continuous variables Kruskal-Wallis test was used for comparing nonparametric distribution among studied groups and the results were described using the median and the interquartile range (IQR). $\chi^2$ test was performed for the categorical variables. Odds ratios for disease outcomes were assessed by univariated logistic regression models. For all tests, a value of $p < 0.05$ was considered statistically significant. The analysis was performed using the STATA v.13 statistical package (StataCorp Texas, USA).

## RESULTS

A total of 722 qRT-PCR confirmed COVID-19 positive individuals were included in this study, of which 9 were excluded. A total of 713 patients were studied, 193 (27%) were classified in mild, 232 in severe (32%), 169 in critical (24%) and 119 (17%) deceased.

The median age was 52 (43-63) years, we found significant differences among outcomes, the mild group were the youngest with a median age of 44 (32-51) years and the deceased group were the oldest with a median age of 63 (54-70) years old. Of the total population study 453 (60%) were male. The critical and deceased group had a higher percentage of male with 121 (72%) and 75 (63%) respectively. The main cardiometabolic comorbidity was overweight N = 221 (31%) *(Table 1)*. Other comorbidities were smoking (17%), cardiopatias (3%), alcoholism (2%) neumopatias (1.6%) and neuropathies (1.5%).

In the total population, the main symptoms were cough (70%), fever (62%), dyspnea (59%) *(Figure 1)*. In the mild group cough, headache and

**Table 1:** Anthropometrics and clinics characteristics of population study.

| | Total (N = 713) | Mild (N = 193) | Severe (N = 232) | Critical (N = 169) | Deceased (N = 119) | p |
|---|---|---|---|---|---|---|
| Age | 52 (43-63) | 44 (32-51) | 53 (43-63.5) | 52.5 (46-63) | 63 (54-70) | < 0.001* |
| Gender male§ | 434 (61) | 94 (49) | 144 (62) | 121 (72) | 75 (63) | < 0.001‡ |
| Overweight§ | 221 (31) | 12 (6) | 91 (39) | 77 (46) | 41 (34) | < 0.001‡ |
| Obesity§ | 215 (30) | 24 (12) | 80 (35) | 70 (41) | 41 (34) | < 0.001‡ |
| Type 2 diabetes§ | 208 (29) | 21 (11) | 79 (34) | 57 (33) | 51 (43) | < 0.001‡ |
| Hypertension§ | 209 (29) | 24 (12) | 72 (31) | 62(37) | 51 (43) | < 0.001‡ |
| Heart rate, median (IQR), bpm+ | 93 (81-106) | 90 (79-101) | 93 (80-105) | 96 (87-110) | 93 (81-105) | 0.002* |
| Oxygen saturation % (IQR) | 88 (80-93) | 94 (92-95) | 87 (80-92) | 82 (72-88) | 80 (70-89) | < 0.001* |

IQR = interquartile range. * Kruskall-Wallis test. ‡ $\chi^2$. § Data expressed in frequency and percentage [n (%)].

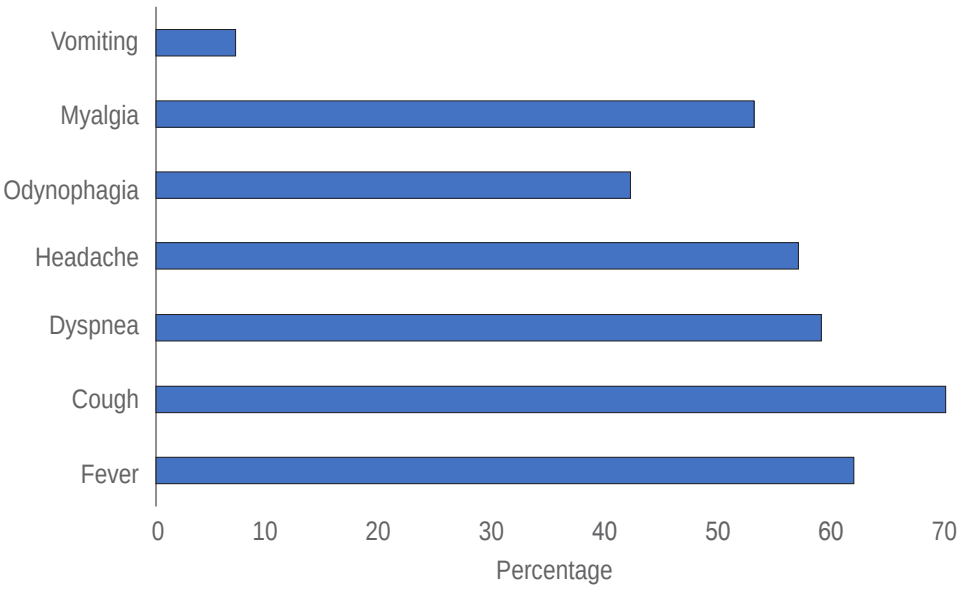


**Figure 1:**

Main symptoms in total population study.

**Table 2:** Odds Ratio for COVID-19 outcomes and main patient features and comorbidities.

| | Severe | 95% CI | p value | Critical | 95% CI | p | Deceased | 95% CI | p |
|---|---|---|---|---|---|---|---|---|---|
| Age | 1.05 | 1.03-1.06 | ≤ 0.001 | 1.06 | 1.04-1.08 | ≤ 0.001 | 1.12 | 1.09-1.15 | ≤ 0.001 |
| Female sex | 0.58 | 0.39-0.85 | 0.006 | 0.37 | 0.24-0.58 | ≤ 0.001 | 0.55 | 0.34-0.88 | 0.01 |
| Type 2 diabetes | 4.22 | 2.49-7.17 | ≤ 0.001 | 4.16 | 2.4-7.3 | ≤ 0.001 | 6.14 | 3.43-10.97 | ≤ 0.001 |
| Hypertension | 1.21 | 0.69-2.1 | 0.49 | 1.49 | 0.84-2.6 | 0.17 | 1.87 | 1.02-3.4 | 0.04 |
| Overweight | 9.73 | 2.23-6.14 | ≤ 0.001 | 12.62 | 6.54-24.3 | ≤ 0.001 | 7.92 | 2.09-6.54 | ≤ 0.001 |
| Obesity | 3.70 | 2.23-6.14 | ≤ 0.001 | 4.97 | 2.94-8.42 | ≤ 0.001 | 3.7 | 2.09-6.54 | ≤ 0.001 |

cough were the main symptoms. Fever, dyspnea and cough were the most frequent symptoms in the severe and critical group, while fever was the main symptom among those who died. We found significant differences in ferritin and lactic dehydrogenase ($p < 0.001$) levels. We observed an increase of ferritin among the groups, the deceased group had the highest levels of ferritin and lactic dehydrogenase with a median of 692.65 ng/mL (IQR 390.6-1213.7) and 408 U/L (IQR 322-493), respectively *(Figure 2)*.

In the univariate analysis we observed that age, type 2 diabetes, overweight and obesity likely increase the risk of developing a worst COVID-19 outcome. For the sex variable, the observed that being a women have a negative association with the development of a fatal outcome for COVID-19 *(Table 2)*.

## DISCUSSION

Several patients with pneumonia of an unknown etiology were reported in December 2019 in Wuhan China, however, it was not until March 2020 that the World Health Organization (WHO) declared that the SARS-CoV-2 infection was causing COVID-19 pandemic. The findings in the present study indicate that the older patients (> 60 years) were more prone to develop fatal outcomes. Likewise, the male gender has been associated with more severe outcomes of COVID-19, in our work males represented 60% of the total population of study and more importantly more than half of the deceased (63%). In previous reports made worldwide, males had been reported as the gender at higher risk for this disease.[7,9,10] This could be explained by the entry receptors that SARS-CoV-2 uses to get into cells, such as ACE2 and TMPRRS2.

These genes are located on the X chromosome and the particular transcription of the *ACE2* gene is regulated by different sex, ACE2 is expressed in testis, however, in ovary is not expressed, this could be protection to females.[11]

In México, overweight, obesity and T2D were the strongest predictor for COVID-19, this is in agreement with the previously reported in 2020 by Hernández-Garduño.[12] These comorbidities present a low grade chronic inflammation producing adipokines and cytokines promoting an adequate scenario for susceptibility to infection such as SARS-CoV-2, and therefore this virus could enhance the pre-existing inflammation resulting in a more severe COVID-19 outcome.[13]

The mortality risk has been reported as increased in patients COVID-19 with intubation requirement,[14] in Mexico, having an age ≥ 60 years and hypertension had been reported like factors risk to death, however, in our study, we found that overweight and T2D were the main mortality risk factors risk, this reflect the public health problem of high prevalence of non-communicable diseases we suffer in Mexico, and the imperious necessity for their control.

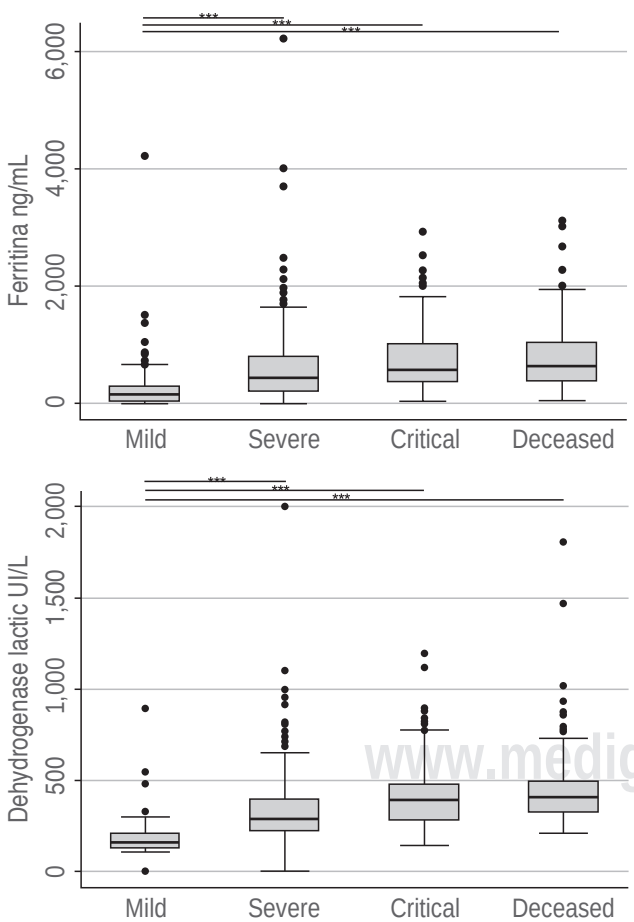


**Figure 2:** Clinics levels among study groups.
* Significance differences.

## References

1. Organization WH. Novel coronavirus -Disease outbreak 2020. 2022.
2. Lai CC, Shih TP, Ko WC, Tang HJ, Hsueh PR. 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. Hopkins J. Coronavirus resource center. 2022. Available in: https://coronavirus.jhu.edu/
4. Kadam SB, Sukhramani GS, Bishnoi P, Pable AA, Barvkar VT. SARS-CoV-2, the pandemic coronavirus: molecular and structural insights. J Basic Microbiol. 2021; 61 (3): 180-202.
5. Palacios Cruz M, Santos E, Velázquez Cervantes MA, León Juárez M. COVID-19, a worldwide public health emergency. Revista Clínica Española. 2021; 221 (1): 55-61.
6. Martinez-Fierro ML, Diaz-Lozano M, Alvarez-Zuñiga C, Ramirez-Hernandez LA, Araujo-Espino R, Trejo-Ortiz PM et al. Population-Based COVID-19 Screening in Mexico: Assessment of Symptoms and Their Weighting in Predicting SARS-CoV-2 Infection. Medicina (Kaunas). 2021; 57 (4): 363.
7. Mesta F, Coll AM, Ramírez M, Delgado-Roche L. Predictors of mortality in hospitalized COVID-19 patients: a Mexican population-based cohort study. Biomedicine (Taipei). 2021; 11 (2): 1-4.
8. Gandhi RT, Lynch JB, Del Rio C. Mild or moderate Covid-19. N Engl J Med. 2020; 383 (18): 1757-1566.
9. Onder G, Rezza G, Brusaferro S. Case-fatality rate and characteristics of patients dying in relation to COVID-19 in Italy. JAMA. 2020; 323 (18): 1775-1776.
10. Fernández-Rojas MA, Luna-Ruiz Esparza MA, Campos-Romero A, Calva-Espinosa DY, Moreno-Camacho JL, Langle-Martínez AP et al. Epidemiology of COVID-19 in Mexico: symptomatic profiles and presymptomatic people. Int J Infect Dis. 2021; 104: 572-579.
11. Li AJ, Li X. Sex-dependent immune response and lethality of COVID-19. Stem Cell Res. 2020; 50: 102116.
12. Hernández-Garduño E. Obesity is the comorbidity more strongly associated for Covid-19 in Mexico. A case-control study. Obes Res Clin Pract. 2020; 14 (4): 375-379.

13. López-Reyes A, Martinez-Armenta C, Espinosa-Velázquez R, Vázquez-Cárdenas P, Cruz-Ramos M, Palacios-González B et al. NLRP3 inflammasome: the stormy link between obesity and COVID-19. Front Immunol. 2020; 11: 570251.

14. Becerra-Sánchez A, Rodarte-Rodríguez A, Escalante-García NI, Olvera-González JE, De la Rosa-Vargas JI, Zepeda-Valles G et al. Mortality analysis of patients with COVID-19 in Mexico based on risk factors applying machine learning techniques. Diagnostics (Basel). 2022; 12 (6): 1396.