*Coronavirus Pandemic*

# Prognostic factors of COVID-19 severity and mortality in the Yucatecan ethnic of México contrast with other populations

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## Abstract

Introduction: Previous studies that identified the prognostic factors for the severity of the new coronavirus disease 2019 (COVID-19) in different populations have generated controversial conclusions. The lack of a standard definition of COVID-19 severity and the differences between clinical diagnoses might make it difficult to provide optimum care according to the characteristics of each population.
Methodology: We investigated the factors that impacted the severe outcome or death from the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in patients treated at the Mexican Institute of Social Security in Yucatán, México in 2020. A cross-sectional study of COVID-19 confirmed cases was done to know the prevalence and association of the demographic and clinical characteristics with a severe or fatal outcome. Information from the National Epidemiological Surveillance System (SINAVE) database was used and SPSS v 21 was used for statistical analyses. We used the World Health Organization (WHO) and the Centers for Diseases Control and Prevention (CDC) symptomatology classifications to define severe cases.
Results: Diabetes and pneumonia increased the risk of death and having diabetes was a prognostic factor for severe illness following SARS-CoV-2 infection.
Conclusions: Our results highlight the influence of cultural and ethnic factors, the necessity to standardize the parameters for clinical diagnoses, and to use the same criteria for the definition of COVID-19 severity to establish the clinical conditions that contribute to the pathophysiology of this disease in each population.

**Key words:** SARS-CoV-2; severity; mortality; comorbidities.

## Introduction

The new coronavirus disease 2019 (COVID-19) is an infectious disease caused by the severe acute respiratory syndrome coronavirus (SARS-CoV-2) which is transmitted from an infected person through small liquid particles generated when they cough, sneeze, speak, sing or breathe [1]. Most people infected with the virus will experience mild to moderate respiratory illness and recover without requiring special treatment. However, some will become seriously ill with acute lower respiratory tract infection leading to respiratory failure and/or multi-organ dysfunction syndrome and death [2,3]. The most common symptoms of COVID-19 are fever, dry cough, and fatigue; other less common symptoms that may affect some patients include loss of taste or smell, nasal congestion, conjunctivitis (red eyes), sore throat, headache, muscle or joint pain, skin rash, nausea, vomiting, diarrhea, chills or dizziness. Symptoms of severe COVID-19 disease include shortness of breath, loss of appetite, confusion, persistent pain or pressure in the chest, irritability, reduced consciousness (sometimes associated with seizures), anxiety, depression, sleep disorders, neurological complications such as strokes, brain inflammation, delirium, and nerve damage [1].

Anyone can get sick with COVID-19 and become seriously ill or die, but older people and those with underlying medical conditions like cardiovascular disease (CVD), diabetes, chronic respiratory disease (CRD), or cancer are more likely to develop a serious illness [1].

The first case of COVID-19 in México was officially reported on February 28, 2020. Since then, several studies spanning different periods of 2020 were carried out to identify the risk factors associated with hospitalization, intensive care, or death from COVID-19. The studies concluded that people with older age,

male gender, diabetes, hypertension, obesity, chronic kidney disease (CKD), immunosuppression, or pneumonia were more likely to be hospitalized or die than people without these conditions [4-9]. This situation was also reported in studies in other countries and some reported different or controversial results [10]. This suggests that different sample sizes and heterogeneity in study design or subjective criteria to classify the severity of the infection may impact the findings.

Although vaccines have reduced the risk of death from COVID-19, surveillance of people over 60 years of age or with diabetes, hypertension, obesity, CKD, or immunosuppression, are still prioritized among the population infected with SARS-CoV-2 hospitalized at the Mexican Institute of Social Security (IMSS) in México. However, the wide cultural and ethnic diversity in the Mexican Republic can influence the impact of comorbidities, especially in populations with very contrasting genetic factors such as in the Yucatán Peninsula where the Mayan culture is concentrated. This population has a diet rich in calories and fat and in 2019 a study highlighted the high incidence of obesity in this population [11].

Thus, we aimed to know the prognostic factors of severe illness and death in SARS-CoV-2 positive cases who attended the IMSS in Yucatán México in 2020. We compared the findings between Mexican people and other countries, infected with the same variant of SARS-CoV-2 and who were not vaccinated to match the conditions.

## Methodology

A cross-sectional and retrospective study of confirmed COVID-19 cases during the period April to November 2020, from the state of Yucatán, that were registered in the IMSS database was carried out. The data included information about non communicable diseases (NCDs), symptomatology, and demographic aspects of the patients, which corresponded to 10% of ambulatory cases and 100% of hospitalized serious cases and deaths. The data were downloaded from the National Epidemiological Surveillance System (SINAVE) platform. Clinical and comorbidities information recorded by physicians at the time of care and hospital admission of patients in the medical system were also included. This study was approved by the National Committee on Ethics and Health Research of the IMSS and registered as R-2020-785-114. The study did not require informed consent because it is based on open, anonymized data from the Mexican Ministry of Health.

Patients who presented mild symptoms were included in the group of non-severe cases, patients with at least 1 severe symptom requiring hospitalization without death were included in the severe group, and patients with severe symptoms who died were included in the deceased group. According to the World Health Organization (WHO) and the Center for Diseases Control and Prevention (CDC), severe COVID-19 symptoms were chest pain, pneumonia, cyanosis, dyspnea, and polypnea [1,12].

All symptoms were coded in a categorical binary method, yes vs. no, if they were present or absent respectively in patients at triage stay or hospital admission. Categorical variables were described as frequencies and percentages. Chi-square tests with Phi value were analyzed for each group of patients to estimate the association between either severity or mortality, and the demographic and clinical conditions of the patients in the groups. The more frequent variables with statistical significance were included in a final binary logistic regression model of each group to find out the odds ratios of the characteristics assessed. All analyses were performed with the statistical package software SPSS v 21 [13]. A *p* value < 0.05 was considered significant.

## Results

We selected 2271 patients with positive SARS-CoV-2 quantitative polymerase chain reaction (qPCR). Among them 56% were men, the majority were in the age group 21-40 years (37.7%), and most of the patients worked as employees (40.6%) or were healthcare workers (25.4%). In addition, 45.6% were outpatients (non-severe group), 27.4% presented severe symptoms but did not die (severe group), and 27% died (Table 1).

Among the patients with mild symptoms, 54% were men, 64.6% were between 21-40 years old, 46.1% were healthcare workers, 42.8% had other types of jobs, and 11.1% had no job (Table 1). Almost half of the patients presented 1 to 5 mild symptoms and the rest presented 6 to 10 mild symptoms of which headache was more frequent followed by fever, cough, and myalgia. Obesity and hypertension were the more frequent comorbidities of this group of patients.

On the other hand, 55% of patients within the severe group were men, 41.5% were between 41 and 60 years of age, and most had jobs other than healthcare or were housewives. This group was characterized by a high frequency of 1 to 5 mild symptoms, mainly fever or cough, along with dyspnea, chest pain, or pneumonia. Hypertension and diabetes were the frequent comorbidities (Table 1).

The group of deceased patients had high frequency of men, age > 60 years, and employees other than healthcare workers. Thirty-three patients did not present mild symptoms, 514 presented 1-5 mild symptoms, and 56 had 6-10 mild symptoms. Major symptoms of this group were dyspnea, along with fever or cough, while hypertension and diabetes were more frequent than those in the serious illness group (Table 1).

Our bivariate and multivariate analyses of each group showed a moderate statistically significant direct association between developing a serious illness and the presence of chest pain, dyspnea, or diabetes, and less association with hypertension. Diabetes conferred 22 times more likelihood of suffering from severe COVID-

**Table 1.** Frequency of demographic data, clinical characteristics, and non-communicable diseases in groups of patients confirmed with coronavirus disease 2019 (COVID-19) who attended the Mexican Institute of Social Security in Yucatán, México.

| Prognostic Factor | Non-severe frequency (%) | Severe frequency (%) | Deceased frequency (%) | Total patients (%) |
|---|---|---|---|---|
| Male | **564 (54)** | **343 (55)** | **363 (59.4)** | 1274 (56) |
| Female | 474 (46) | 279 (45) | 248 (40.6) | 1002 (44) |
| Student | 32 (3.1) | 2 (0.3) | 0 | 34 (1.5) |
| Health Care | **478 (46.1)** | 89 (14.3) | 4 (0.7) | 576 (25.4) |
| Employee | **444 (42.8)** | 291 (46.8) | **187 (30.6)** | 922 (40.6) |
| Retired | 16 (1.5) | 96 (15.4) | **220 (36.0)** | 332 (14.6) |
| Informal | 28 (2.8) | 29 (4.7) | 48 (7.9) | 123 (5.4) |
| Housewife | 40 (4) | **104 (16.7)** | 145 (23.7) | 289 (12.7) |
| 0-20 years old | 28 (2.7) | 4 (0.8) | 3 (0.5) | 35 (1.5) |
| 21-40 years old | **671 (64.6)** | 165 (26.5) | 22 (3.6) | 859 (37.7) |
| 41-60 years old | 305 (29.4) | **258 (41.5)** | 143 (23.4) | 710 (31.1) |
| > 60 years old | 34 (3.3) | 195 (31.4) | **443 (72.5)** | 672 (29.5) |
| Antipyretic | **503 (48.5)** | 152 (24.4) | 68 (11.1) | 723 31.8 |
| Flu vaccine | **306 (29.3)** | 64 (10.3) | 16 (2.6) | 386 17 |
| Fever | **800 (77)** | 512 (82.3) | 457 (74.8) | **1769 78** |
| Cough | **762 (73)** | 453 (72.8) | 407 (66.6) | **1622 71.4** |
| Headache | **878 (84.6)** | 353 (56.8) | 245 (40.1) | **1476 65** |
| Odinophagia | 586 (56.5) | 209 (33.6) | 97 (15.9) | 892 39.3 |
| Myalgia | **759 (72.8)** | 306 (49.2) | 149 (24.4) | **1214 53.4** |
| Arthralgia | 581 (56) | 263 (42.3) | 127 (20.8) | 971 42.7 |
| Rhinorrhea | 339 (32.7) | 103 (16.6) | 41 (6.7) | 483 21.3 |
| Chills | 223 (21.5) | 87 (14) | 34 (5.6) | 344 15.1 |
| Abdominal pain | 45 (4.3) | 31 (5) | 31 (5.1) | 107 4.7 |
| Conjunctivitis | 40 (4) | 18 (2.9) | 7 (1.1) | 65 2.8 |
| Diarrhea | 190 (18.3) | 129 (20.7) | 74 (12.1) | 393 17.3 |
| Anosmia | 332 (32) | 114 (18.3) | 43 (7.0) | 489 21.5 |
| Dysgeusia | 326 (31.4) | 114 (18.3) | 50 (8.2) | 490 21.6 |
| Chest pain | 0 | **227 (36.5)** | **101 (16.5)** | 328 14.4 |
| Cyanosis | 0 | 5 (0.8) | 22 (3.6) | 27 1.2 |
| Dyspnea | 0 | **495 (79.6)** | **586 (95.9)** | 1081 47.6 |
| Polypnae | 0 | 8 (1.3) | 24 (3.9) | 32 1.4 |
| Pneumonia | 0 | **96 (15.4)** | **309 (50.6)** | 405 17.8 |
| COPD | 2 (0.2) | 11 (1.8) | 22 (3.6) | 35 (1.5) |
| Smoking | 62 (5.9) | 27 (4.3) | 16 (2.6) | 108 (4.7) |
| Diabetes | 65 (6.3) | **177 (28.5)** | **263(43.0)** | **505 (22.2)** |
| Asthma | 51 (5) | 25 (4.0) | 15 (2.5) | 91 (4) |
| Obesity | **187 (18)** | 86 (13.8) | 54 (8.8) | 327 (14.4) |
| HIV infection | 6 (0.6) | 4 (0.6) | 2 (0.3) | 12 (0.53) |
| Hypertension | **184 (17.7)** | **214 (34.4)** | **314 (51.4)** | **714 (31.4)** |
| CVD | 9 (0.9) | 25 (4.0) | 40 (6.5) | 74 (3.2) |
| Tuberculosis | 2 (0.2) | 1 (0.2) | 1 (0.2) | 4 (0.13) |
| Cancer | 2 (0.2) | 6 (1.0) | 9 (1.5) | 17 (0.7) |
| CKD | 4 (0.4) | 21 (3.4) | 74 (12.1) | 99 (4.3) |
| CLD | 0 | 4 (0.6) | 14 (2.3) | 18 (0.8) |
| Hemolytic anemia | 0 | 1 (0.2) | 1 (0.2) | 2 (0.04) |
| Neurologic disease | 1 (0.1) | 4 (0.6) | 13 (2.1) | 18 (0.8) |
| Total | 1038 | 622 | 611 | 2271 |

COPD: chronic obstructive pulmonary disease; HIV: human immunodeficiency virus; CKD: chronic kidney disease; CLD: chronic liver disease; CVD: cardiovascular disease.

19 (Table 2). Regarding mortality from COVID-19, a low association was found with pre-existing diabetes, hypertension, the presence of dyspnea, or pneumonia, of which diabetes and pneumonia were the major prognostic factors for death (Table 3).

## Discussion

In this study, SARS-CoV-2 infection was classified as mild and severe based on the symptomatology taken into account by the WHO and the CDC classification [1,12], instead of the different criteria used to classify the severity of the disease in the previous literature on COVID-19.

We found that gender did not contribute to the severity or mortality, contrary to what was reported in a large Mexican population [4,6-9].

Previous studies in México showed that among the patients who attended IMSS those over 60 years of age had a high risk of death due to COVID-19 [4,5,7]. Nevertheless, in our study, we found that individuals over 40 years of age more commonly had severe cases and those over 60 years of age were not associated with lethal COVID-19.

Hypertension and diabetes were the most frequent comorbidities associated with severe disease. However, only diabetes was a risk factor that increased the chance

of severity or fatal outcome of COVID-19 in our population [4-9] and other populations worldwide [14-16]. Conversely, in a global study, hypertension, diabetes, and CKD showed no significant elevated risk for COVID-19 severity [10]. However, patients with CKD had a high prevalence of comorbidities, such as hypertension, CVD, and diabetes mellitus, which might contribute to severe outcomes among these patients [17].

We found that the presence of other pre-existing NCDs was not associated with the severity or mortality of COVID-19, such as COPD and CVD which were not associated with death in patients with COVID-19 in México [5], although CVD was a prognostic factor for complications (pneumonia and intubation) or death in COVID-19 patients in Nuevo León, México [8], while COPD was reported as a prognostic factor for intensive care unit (ICU) admission, invasive ventilation, and death in COVID-19 patients in other countries [18].

On the other hand, obesity was more frequent in patients with mild illnesses than in those with serious illnesses or who died. Therefore, contrary to what has been reported in many populations, obesity was not associated with severe or lethal COVID-19 probably because of the high prevalence of this condition among

**Table 2.** Association between demographic data, clinical characteristics, or non-communicable diseases and coronavirus disease 2019 (COVID-19) severity in patients who attended the Mexican Institute of Social Security in Yucatán, México.

| Prognostic factor | Frequency % | Pearson's X² | Fisher's exact sig | PHI | OR | CI 95% lower | CI 95% higher | BLR sig |
|---|---|---|---|---|---|---|---|---|
| Male | 55 | 0.10 | 0.76 | 0.01 | -- | -- | -- | -- |
| Antipyretics | 39 | 94 | 0.00 | -0.24 | 0.2 | 0.1 | 0.3 | 0.000 |
| Flu vaccine | 22 | 81.3 | 0.00 | -0.22 | 1.7 | 0.8 | 4 | 0.188 |
| 21-40 years old | 50 | 1009 | 0.00 | -0.78 | 1 | 0 | 0 | 0.993 |
| 41-60 years old | 34 | 510.5 | 0.00 | -0.55 | 1.4 | 0 | 0 | 0.992 |
| >60 years old | 14 | 159.2 | 0.00 | -0.31 | 0.9 | 0 | 0 | 1 |
| Health care | 34 | 516 | 0.00 | -0.56 | 0.8 | 0 | 0 | 0.983 |
| Employee | 44 | 790.4 | 0.00 | -0.69 | 1.1 | 0 | 0 | 0.997 |
| 1-5 mild symptoms | 58 | 1381 | 0.00 | -0.91 | 0 | 0 | 0 | 0.992 |
| 6-10 mild symptoms | 40 | 661.5 | 0.00 | -0.63 | 0.7 | 0 | 0 | 1 |
| Fever | 79 | 6.45 | 0.01 | 0.06 | 0.4 | 0.08 | 1.8 | 0.226 |
| Cough | 73 | 0.07 | 0.82 | -0.01 | -- | -- | -- | -- |
| Headache | 74 | 155.6 | 0.00 | -0.31 | 0.2 | 0.05 | 1 | 0.064 |
| Odinophagia | 48 | 81.4 | 0.00 | -0.22 | 1.7 | 0.3 | 8 | 0.524 |
| Myalgia | 64 | 96.8 | 0.00 | -0.24 | 0.2 | 0.03 | 0.9 | 0.033 |
| Arthralgia | 51 | 29.2 | 0.00 | -0.13 | 0.3 | 0.02 | 4.2 | 0.388 |
| Rhinorrhea | 27 | 51.6 | 0.00 | -0.18 | 0.2 | 0.03 | 2.4 | 0.227 |
| Chills | 19 | 14.4 | 0.00 | -0.1 | 0 | 0 | 0 | 0.988 |
| Diarrhea | 19 | 1.5 | 0.22 | 0.03 | -- | -- | -- | -- |
| Anosmia | 27 | 37 | 0.00 | -0.15 | 0 | 0 | 0 | 0.987 |
| Dysgeusia | 26 | 34 | 0.00 | -0.14 | 0 | 0 | 0 | 0.966 |
| Chest Pain | 14 | 439 | 0.00 | 0.51 | 0 | 0 | 0 | 0.98 |
| Dyspnea | 30 | 1177 | 0.00 | 0.84 | 0 | 0 | 0 | 0.99 |
| Diabetes | 15 | 153.8 | 0.00 | 0.30 | 22 | 5 | 98 | 0.000 |
| Obesity | 16 | 5 | 0.03 | -0.05 | 1.6 | 0.2 | 16 | 0.666 |
| Hypertension | 24 | 59.3 | 0.00 | 0.19 | 0.5 | 0.08 | 3.7 | 0.546 |

OR: odds ratio; BLR: binary logistic regression; sig: significance. Null data are marketed with dashes.

the Yucatecan population which does not depend on age or social status.

Similar or contradictory findings were observed by others, in México [4-6,8,9] or in other countries [10,16,18].

We showed that pneumonia had an increased risk of COVID-19 mortality, similar to other studies with the Mexican population [5-7,9]. In contrast, the risk of COVID-19 mortality was highest with the presence of dyspnea or cyanosis in hospitalized or critically ill patients with COVID-19 in Wuhan and Washington [19-21], and elderly [22] or cancer patients diagnosed with COVID-19 [23] suggesting that age and immunosuppression could have influenced the development of severe symptoms and mortality after SARS-CoV-2 infection.

Similar to other studies [16,18], we did not find statistically significant differences between the proportion of patients with myalgia, arthralgia, headache fever, cough, fatigue, diarrhea, nausea, or abdominal pain at hospital admission in people with severe symptoms or survivors of COVID-19 compared with the patients with non-severe ill or deceased, although Booth *et al.* [10] suggested myalgia and chills as prognostic factors for the severe disease.

Immunosuppression, HIV infection, asthma, and smoking did not have any association with the clinical form of COVID-19 among the Yucatecan people, but similar or contradictory findings were also observed in the other studies in México and other countries [4-6,8]. Nevertheless, since multiple factors can cause immunosuppression, the lack of defined criteria to classify immunodeficiency in all medical units of México could lead to underreporting of immunosuppressed patients in Yucatán.

Regarding asthma and smoking, we observed no significant contribution to mortality in our population with COVID-19 coinciding with previous findings in other studies with more patients attending the IMSS being included [5,9].

However, in a large data set of Mexican populations asthma was found to be a protective factor against hospitalization, intubation, and death. Smoking was also a protective factor against hospitalization and admission to the ICU, but no significant association was found with intubation [4].

Furthermore, smoking was a protective factor against pneumonia and death in Nuevo León México, but asthma showed a consistent risk association for complications leading to pneumonia and death [8] and with severe or critical illness [24].

**Table 3.** Association between demographic data, clinical characteristics, or non-communicable diseases and coronavirus disease 2019 (COVID-19) mortality of patients who attended the Mexican Institute of Social Security in Yucatán, México.

| Prognostic factor | Frequency % | Pearson's $X^2$ | Fisher's exact sig | PHI | OR | CI 95% lower | CI 95% higher | BLR sig |
|---|---|---|---|---|---|---|---|---|
| Male | 57 | 2.3 | 0.13 | 0.04 | -- | -- | -- | - |
| Antipyretics | 18 | 37.2 | 0.000 | -0.17 | 2.4 | 0.8 | 7 | 0.123 |
| 21-40 years old | 15 | 216.5 | 0.000 | -0.42 | 0 | 0 | 0 | 0.994 |
| 41-60 years old | 32 | 605 | 0.000 | 0.70 | 0 | 0 | 0 | 1.00 |
| > 60 years old | 52 | 1170.6 | 0.000 | -1 | 0 | 0 | 0 | 0.982 |
| Housewife | 20 | 306.5 | 0.000 | -0.50 | 0 | 0 | 0 | 1.00 |
| Employee | 39 | 20.6 | 0.000 | -0.13 | 0 | 0 | 0 | 0.991 |
| 1-5 mild symptoms | 77 | 382.5 | 0.000 | -0.56 | 0.9 | 0.9 | 0 | 1.00 |
| 6-10 mild symptoms | 18 | 267.4 | 0.000 | -0.47 | 0 | 0 | 0 | 0.994 |
| Fever | 79 | 10.4 | 0.001 | -0.1 | 0.7 | 0.2 | 3.2 | 0,672 |
| Cough | 70 | 5.6 | 0.019 | -0.07 | 3.3 | 0.7 | 15 | 0.123 |
| Headache | 49 | 34.9 | 0.000 | -0.17 | 0.5 | 0.2 | 1.7 | 0.307 |
| Odinophagia | 25 | 52 | 0.000 | -0.20 | 1 | 0.3 | 4 | 0.993 |
| Myalgia | 37 | 81.5 | 0.000 | -0.26 | 0.5 | 0.13 | 2.1 | 0.366 |
| Arthralgia | 32 | 65.9 | 0.000 | -0.23 | 1.2 | 0.2 | 8.2 | 0.863 |
| Rhinorrhea | 12 | 29 | 0.000 | -0.15 | 1.5 | 0.3 | 6.2 | 0.587 |
| Chills | 10 | 24.7 | 0.000 | -0.14 | 1.6 | 0.2 | 12 | 0.634 |
| Diarrhea | 16 | 16.7 | 0.000 | -0.12 | 0.7 | 0.14 | 4 | 0.737 |
| Anosmia | 13 | 35.3 | 0.000 | -0.17 | 0 | 0 | 0 | 0.990 |
| Dysgeusia | 13 | 27.5 | 0.000 | -0.15 | 0 | 0 | 0 | 0.990 |
| Chest Pain | 27 | 63 | 0.000 | -0.23 | 0.5 | 0.14 | 2.1 | 0.376 |
| Dyspnea | 88 | 76 | 0.000 | 0.25 | 0 | 0 | 0 | 0.990 |
| Diabetes | 36 | 28.6 | 0.000 | 0.15 | 3.5 | 1 | 11 | 0.032 |
| Obesity | 11 | 7.6 | 0.007 | -0.08 | 3 | 0.6 | 12 | 0.203 |
| Hypertension | 43 | 36.3 | 0.000 | 0.17 | 1.7 | 0.6 | 5.2 | 0.343 |
| Pneumonia | 33 | 172.5 | 0.000 | 0.37 | 3 | 1.2 | 9.3 | 0.024 |

OR: odds ratio; BLR: binary logistic regression; sig: significance. Null data are marketed with dashes.

## Conclusions

The influence of cultural and ethnic factors, standardized parameters for clinical diagnoses, and classification of COVID-19 severity are important factors to consider when formulating the measures of containment and management of the patients in order to avoid complications from COVID-19 in each population.

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