Mortality Rate of Patients with COVID-19 Based on Underlying Health Conditions

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Running title: Mortality Rate of Patients with COVID-19
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Abstract
Objective: To evaluate the mortality rates of 566,602 patients with coronavirus disease (COVID-19) based on sex, age, and the presence or absence of underlying diseases and determine whether the underlying disease provides prognostic information specifically related to death.

Methods: The mortality rate was evaluated using conditional probability to identify the significant factors, and adjusted odds ratios (ORs) using a multivariable logistic regression analysis were estimated.

Results: The mortality rate of patients with underlying health conditions was 12%, which was 4 times higher than that of patients without underlying health conditions. Furthermore, the mortality rates of women and men with underlying health conditions were 5.5 and 3.4 times higher than the mortality rates of patients without underlying health conditions, respectively. In a multivariable logistic regression analysis including sex, age, and underlying health conditions, male sex (OR: 1.83), age ≥ 41 years (ORs > 2.70), and underlying health conditions (OR: 2.20) were confirmed as risk factors for death.

Conclusions: More attention should be paid to older patients with underlying diseases and male patients with underlying diseases as the probability of death in this population was significantly high.

Keywords: COVID-19; mortality rate; underlying disease; health condition

Abbreviation List
CKD: Chronic kidney disease
COPD: Chronic obstructive pulmonary disease
COVID-19: Coronavirus disease 2019
INTRODUCTION

Coronavirus disease 2019 (COVID-19) was first identified in December 2019 in Wuhan, China. In May 2020, the World Health Organization declared COVID-19 a pandemic. By February 3, 2021, SARS-CoV-2 (the virus that causes the disease COVID-19) had spread to 223 countries with a mortality rate of 2.2%. Generally, COVID-19 is more severe in people aged >60 years or those with underlying diseases. Research on COVID-19 has been conducted from various perspectives, such as infection cases, clinical characteristics, and preventive measures. In addition, several studies have confirmed that COVID-19 is more severe in older people and those with underlying diseases, such as lung or heart disease, diabetes, and immunological diseases. The Mexican government provides information on several confirmed cases (566,602 patients), and studies on clinical significance and validation based on these data have been conducted. However, existing studies have targeted relatively few cases (less than 1,000 cases), and comparative analysis of the association between the presence or absence of an underlying disease and the mortality rate based on age or sex remains inadequate. COVID-19 data from Mexico include many confirmed cases and 23 variables, including sex, age, date of symptom onset and death, and underlying disease status. Therefore, we can use these data to compare and analyze the mortality rates according to underlying diseases, age, and sex and obtain relevant information. In this study, we evaluated the effect of COVID-19 on mortality rate in patients with underlying health conditions; moreover, we presented the probability values of mortality rate based on nine underlying diseases, age, and sex. Furthermore, we determined the age-specific mortality rate and the mortality rate based on the presence or absence of underlying health conditions in each age group.

METHODS

DATA SOURCE

We retrospectively analyzed the data provided by the Mexican government to evaluate the mortality rate of COVID-19 patients and identify important variables influencing mortality. The data of 566,602 patients included 23 parameters, such as sex, age, symptom onset date, death date, and nine underlying health conditions, including diabetes, chronic obstructive pulmonary disease (COPD), asthma, immunosuppression,
hypertension, chronic kidney disease (CKD), cardiovascular disease, obesity, and other diseases; these data were collected from January 1, 2020, to May 31, 2020.

**DATA ANALYSIS**

Conditional probability was calculated to ascertain the mortality rate for each factor. The chi-square test was used to determine whether the presence or absence of an underlying disease had a significant effect on the mortality rate. Continuous variables are presented as mean (standard deviation). Welch’s t-test or Student’s t-test was used to describe the difference in time intervals depending on the presence or absence of the underlying health condition. In multivariate logistic regression analysis, the odds ratio (OR) was estimated for the mortality rate based on sex, age, and the underlying disease. All statistical analyses were performed using R (version 4.0.2) software, and values of $p < 0.05$ were considered statistically significant.

**RESULTS**

**BASIC CHARACTERISTICS OF CONFIRMED CASES**

Of the 566,602 patients, 287,112 (50.7%) were men, and 279,490 (49.3%) were women, and 36,176 (6.38%) patients had died. In addition, 212,910 (37.6%) had underlying diseases, whereas 353,692 (62.4%) had no underlying diseases; moreover, some patients had comorbidities (Table 1, Fig. 1).

**MORTALITY RATE BASED ON SEX, AGE, AND UNDERLYING HEALTH CONDITIONS**

Figure 1 shows the mortality rate based on sex and the presence or absence of underlying health conditions. The proportion of COVID-19 patients without underlying health conditions was higher than that of patients with underlying health conditions; however, the mortality rate was higher in COVID-19 patients with underlying health conditions. In other words, the probability of death for patients with underlying health conditions, $P(\text{Deaths|Yes})$, was 0.12, which was 4 times higher than that of patients with no underlying health conditions, $P(\text{Deaths|No})=0.03$. Specifically, the proportion of COVID-19 patients with and without underlying health conditions was 37.6% and 62.4%, respectively; however, 70.4% of the total number of deaths occurred in patients with underlying health conditions, and only 29.6% of deaths occurred in patients without an underlying disease ($P(\text{Yes|Deaths})=0.704$, $P(\text{No|Deaths})=0.296$). The mortality rate was 1.8 times as high in men (8.18%) than in women (4.54%). The
proportions of men (50.7%) and women (49.3%) among the study participants were similar; however, 64.9% and 35.1% of deaths occurred in men and women, respectively (P[Male|Deaths]=0.649, P[Female|Deaths]=0.351). The average ages of discharged and deceased patients with COVID-19 were 41.4 (±16.0) years and 60.8 (±15.4) years, respectively. Expressly, patients with COVID-19 who died were approximately 20 years older than those who survived. Therefore, age was an important determining factor of the mortality rate. Hence, we evaluated the mortality rates of the following age groups: 0-20, 21-30, 31-40, 41-50, 51-60, 61-70, 71-80, 81+ years.

Figure 2 shows the mortality rates by age group and the presence or absence of underlying disease. Although there were more patients with COVID-19 in the age groups 21-30, 31-40, and 41-50, more deaths occurred in the age groups 51-60, 61-70, 71-80, and 81+. Regarding only the mortality rate (P[Deaths|No] + P[Deaths|Yes]), it was higher in people aged over 51 years; however, the trend of rates varied by age group as well as the presence or absence of disease. Similarly, the proportion of discharged patients (cured), \[ \frac{P(\text{Cure}|\text{No})}{P(\text{Cure}|\text{No}) + P(\text{Deaths}|\text{No})} \] or \[ \frac{P(\text{Cure}|\text{Yes})}{P(\text{Cure}|\text{Yes}) + P(\text{Deaths}|\text{Yes})} \] differ based on the age group and the presence or absence of an underlying disease.

Table 2 shows the mortality rate and the average time interval owing to the underlying disease, separated by sex and age. The average mortality rate was 6.38%, and the average time interval from symptom onset to death was 10.3 (±6.29) days. The time intervals from symptom onset to death of patients with and without underlying health conditions were 10.1 (±6.23) and 10.7 (±6.42) days, respectively. The \( p \)-value of Welch's \( t \)-test was < .0001, and the time intervals of the two groups were statistically significantly different.

**Sex**

The mortality rates of women and men with COVID-19 were 4.54% and 8.18%, respectively; therefore, mortality rate was sex-related. Women with underlying diseases had a mortality rate of 9.27%, which was 5.5 times higher than that of women without underlying diseases (1.68%). The mortality rate of men with underlying diseases was 14.61%, which was 3.4 times higher than that of men without underlying diseases (4.32%).

**Age**
The 21-30 age group had the lowest mortality rate (0.67%); further, the mortality rates for the 51-60, 61-70, 71-80 and 81+ age groups were 9.93%, 19.67%, 28.02%, and 29.17%, respectively. Furthermore, in all age groups, the mortality rate of patients with underlying health conditions was higher than that of those without underlying health conditions. The mortality rate of patients aged ≤ 60 years with underlying health conditions was at least twice as high as that of patients without underlying health conditions. However, patients aged ≥ 71 years were less affected by underlying health conditions than other age groups.

Underlying Health Conditions
The mortality rate of diabetic patients was 18.71%, which was 4 times higher than that of patients without diabetes (4.59%). Additionally, the mortality rate of patients with underlying diseases was 2.5-4 times higher than that of patients without underlying diseases, excluding asthma. Moreover, the mortality rates of obese patients with and without underlying diseases were 9.15% and 5.81%, respectively.

Time Intervals
Time intervals were defined as the disease durations from initial symptom onset to death. The means and standard deviations of the time interval based on sex, age group, and the presence or absence of underlying health conditions are shown in Table 2 and Table 3. The t-test was performed to evaluate the time intervals for each factor. We observed significant differences in time intervals for the following factors: diabetes, COPD, immunosuppression, hypertension, CKD, cardiovascular disease, other diseases, the 31-40, 41-50, 51-60, 61-70, and 71-80 age groups, and male sex. However, no significant differences in time intervals were observed between the 0-20, 21-30, and 81+ age groups and the female sex (p > .05).

MULTIVARIABLE LOGISTIC REGRESSION
A multivariable logistic regression analysis that included sex, age, and underlying health conditions showed that men had a 1.83 higher OR (95% confidence interval (CI): 1.79-1.88) for mortality rate than women (Table 4). The OR positively correlated with age, indicating that the patient’s age was significantly related to the high COVID-19 mortality rate; ORs > 2.70 in ≥ 41 years group. The OR for patients with underlying diseases was 2.20 (95% CI: 2.15-2.26), implying that the mortality rate of patients with underlying disease increases by at least 2.15 times.
LIMITATIONS

A limitation to this study is that the results cannot be generalized because it was based on a retrospective analysis of COVID-19 patients in Mexico. Since our research focused on underlying health conditions rather than factors, such as ethnicity, socioeconomic deprivation, and culture, a careful approach and interpretation of the study results is required.

DISCUSSION

To date, COVID-19 has spread to 223 countries with a mortality rate of 2.2%. Although many studies have been conducted on this virus, only a few focused on the correlation between underlying health conditions and mortality rate. Among the study participants, 37.6% had underlying health conditions, with a 4 times higher risk of death than patients without underlying diseases. Although the incidence of COVID-19 was similar between men and women, we observed an approximately 2-fold mortality rate in men (64.9%) compared to women (35.1%). This implies that COVID-19 could be more severe in men, and this is consistent with the findings of Clark et al.\textsuperscript{2} and McCullough et al.\textsuperscript{16} Furthermore, the mortality rates of women and men with underlying diseases were 5.5 and 3.4 times higher than the mortality rates of women and men without underlying diseases, respectively. In a multivariable logistic regression that included sex, age, and underlying health conditions, we similarly confirmed that the male sex (OR 1.83) and underlying health conditions (OR 2.20) were risk factors for death.

In this study, we used the data of 566,602 patients with COVID-19, which were considerably large compared to those of Chen et al.\textsuperscript{8}, Kang\textsuperscript{11}, McCullough et al.\textsuperscript{16}, and Zhang et al.\textsuperscript{17}, who studied the correlation between underlying disease and COVID-19; thus, the reliability of our study results is somewhat adequate. Patients with underlying health conditions could be at increased risk of COVID-19, and this risk varies considerably with age. The mortality rate of patients with underlying health conditions increased rapidly in the 41-50, 51-60, and 61-70 age groups, whereas patients aged ≥ 71 years were less likely to be affected by underlying conditions. In addition, the mortality rates of patients with diabetes, COPD, immunosuppression, hypertension, CKD, cardiovascular disease, and other diseases were approximately 2.5-4 times higher than those without underlying conditions. However, in cases of asthma and obesity, no
significant differences were observed in mortality rates. Except for those over 71 years of age, the mortality rate of patients with underlying health conditions was more than 2 times higher than that for patients without underlying conditions. However, patients over 71 years of age were less affected by their underlying health conditions, implying that age is a more important factor than the underlying disease for patients over 71 years.

The time from initial symptom onset to death (time interval) was reduced by the following underlying factors: diabetes, COPD, immunosuppression, hypertension, CKD, cardiovascular disease, and other diseases. This was probably because of the deteriorating state of health due to the disease. Thus, COVID-19 patients with underlying diseases are recommended a comprehensive assessment at early diagnosis due to their vulnerability.

**CONCLUSIONS**

We observed that COVID-19 patients with underlying diseases, male patients, and those above 41 years have an increased risk of death. Particularly, age was confirmed as the most important factor positively correlated with mortality rather than the presence or absence of underlying diseases in those aged above 71 years. Hence, more attention should be paid to older and male patients since the probability of death can be significantly high. In addition, COVID-19 patients with no underlying diseases could have a decreased risk of death. Although our estimates include uncertainty, they provide relevant information regarding the group of patients to place on further observation.

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**Conflicts of interest**
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Figure 1. Mortality rates based on sex and the presence or absence of underlying health conditions. **Fig. 1(left):** the mortality rate for men higher than for women. **Fig. 1(right):** a contrast between the number of deaths of patients with and without underlying diseases.
Figure 2. Mortality rates of age groups based on the presence or absence of underlying health conditions
Table 1. Base characteristics of confirmed cases

|                             | Confirmed (%) | Deaths (%)  |
|-----------------------------|---------------|-------------|
| **Overall**                 | 566,602(100)  | 36,176(6.38)|
| **Sex**                     |               |             |
| Female                      | 279,490(49.3) | 12,696(2.24)|
| Male                        | 287,112(50.7) | 23,480(4.14)|
| **Age**                     |               |             |
| Mean (S.D.)                 | 42.6(±16.7)   | 60.8(±15.4) |
| 0-20                        | 34,709(6.1)   | 455(0.08)   |
| 21-30                       | 103,492(18.3) | 690(0.12)   |
| 31-40                       | 136,498(24.1) | 2085(0.37)  |
| 41-50                       | 122,707(21.7) | 5149(0.91)  |
| 51-60                       | 87,476(15.4)  | 8690(1.53)  |
| 61-70                       | 46,940(8.3)   | 9234(1.63)  |
| 71-80                       | 23,640(4.2)   | 6623(1.17)  |
| 81+                         | 11,140(2.0)   | 3250(0.57)  |
| **Underlying health condition** |             |             |
| No                          | 353,692(62.4) | 10,694(1.89)|
| Yes                         | 212,910(37.6) | 25482(4.50)|
| Diabetes                    | 70,831(12.5)  | 13251(2.34) |
| COPD                        | 9,013(1.6)    | 2033(0.36)  |
| Asthma                      | 18,026(3.2)   | 737(0.13)   |
| Immunosuppression           | 8,978(1.6)    | 1364(0.24)  |
| Hypertension                | 92,508(16.4)  | 15136(2.67) |
| CKD                         | 11,250(2.0)   | 2786(0.49)  |
| Cardiovascular disease      | 12,775(2.3)   | 2219(0.39)  |
| Obesity                     | 92,272(16.3)  | 8444(1.49)  |
| Other disease               | 17,084(3.0)   | 2265(0.40)  |

Note: Underlying health condition=Yes indicates patients with diabetes, COPD, asthma, immunosuppression, hypertension, CKD, cardiovascular disease, obesity, or other diseases

Note: Some patients have comorbidities

CKD: Chronic kidney disease
COPD: Chronic obstructive pulmonary disease
Table 2. Mortality rate of patients based on sex, age group, and underlying health condition, and the average time interval between initial symptom onset and death

| Underlying health condition = Yes or No | Mortality rate (%) | Time intervals (days) | p value |
|----------------------------------------|--------------------|-----------------------|---------|
|                                        | P(Deaths|Yes) | P(Deaths|No) | p value | Yes(Mean ± SD) | No(Mean ± SD) | p value |
| Overall                                | 6.38     | 11.97   | 3.02    | < .0001 | 10.1 ± 6.23   | 10.7 ± 6.42   | < .0001 |
| Sex                                    |          |         |         |         |                |                |         |
| Female                                 | 4.54     | 9.27    | 1.68    | < .0001 | 9.89 ± 6.17   | 10.1 ± 6.50   | .0770 |
| Male                                   | 8.18     | 14.61   | 4.32    | < .0001 | 10.3 ± 6.26   | 10.9 ± 6.37   | < .0001 |
| Age group                              |          |         |         |         |                |                |         |
| 0-20                                   | 1.31     | 3.98    | 0.81    | .4146   | 7.6 ± 6.83    | 7.07 ± 6.20   | .8051 |
| 21-30                                  | 0.67     | 2.03    | 0.34    | .5594   | 8.83 ± 6.15   | 9.61 ± 6.53   | .0548 |
| 31-40                                  | 1.53     | 3.28    | 0.87    | .0088   | 9.82 ± 6.10   | 10.5 ± 6.19   | .0037 |
| 41-50                                  | 4.20     | 6.87    | 2.44    | < .0001 | 10.4 ± 6.22   | 11.2 ± 6.53   | < .0001 |
| 51-60                                  | 9.93     | 13.06   | 6.50    | < .0001 | 10.5 ± 6.28   | 11.2 ± 6.41   | < .0001 |
| 61-70                                  | 19.67    | 22.25   | 14.88   | < .0001 | 10.5 ± 6.30   | 10.9 ± 6.42   | .0031 |
| 71-80                                  | 28.02    | 29.66   | 23.72   | < .0001 | 9.86 ± 6.05   | 10.4 ± 6.36   | .0009 |
| 81+                                    | 29.17    | 30.85   | 25.08   | < .0001 | 9.07 ± 6.02   | 9.22 ± 5.95   | .2790 |

Note: Underlying health condition = Yes indicates patients with diabetes, COPD, asthma, immunosuppression, hypertension, CKD, cardiovascular disease, obesity, or other diseases

Note: Some patients have comorbidities

SD: Standard deviation
Table 3. Mortality rate of patients based on the presence or absence of underlying disease, and the average time interval between initial symptom onset and death.

| Underlying health condition | Mortality rate (%) | Time intervals (days) |  |
|-----------------------------|--------------------|-----------------------|---|
|                             | P(Deaths|Yes)   | P(Deaths|No)   | p value  | Yes(Mean ± SD) | No(Mean ± SD) | p value  |
| Diabetes                    | 18.71              | 4.59                  | < .0001  | 9.89 ± 6.12    | 10.6 ± 6.36   | < .0001  |
| COPD                        | 22.27              | 6.10                  | < .0001  | 9.21 ± 6.05    | 10.4 ± 6.29   | < .0001  |
| Asthma                      | 4.09               | 6.43                  | < .0001  | 10.5 ± 6.26    | 10.3 ± 6.28   | .8390    |
| Immunosuppression           | 15.19              | 6.22                  | < .0001  | 9.14 ± 6.36    | 10.4 ± 6.28   | < .0001  |
| Hypertension                | 16.36              | 4.40                  | < .0001  | 10 ± 6.15      | 10.5 ± 6.37   | < .0001  |
| CKD                         | 24.76              | 5.99                  | < .0001  | 8.81 ± 5.98    | 10.4 ± 6.29   | < .0001  |
| Cardiovascular disease      | 17.37              | 6.10                  | < .0001  | 9.3 ± 6.28     | 10.4 ± 6.28   | < .0001  |
| Obesity                     | 9.15               | 5.81                  | < .0001  | 10.4 ± 6.13    | 10.3 ± 6.33   | .1451    |
| Other diseases              | 13.26              | 6.13                  | < .0001  | 9.62 ± 6.44    | 10.4 ± 6.27   | < .0001  |

Note: Some patients have comorbidities

CKD: Chronic kidney disease

COPD: Chronic obstructive pulmonary disease

SD: Standard deviation
Table 4. Univariate and multivariate analyses for mortality rate: adjusted odds ratios and their 95% confidence intervals based on sex, age, and underlying health condition

|                  | Univariate Unadjusted OR (95% CI) | p value | Multivariate Adjusted OR (95% CI) | p value |
|------------------|-----------------------------------|---------|-----------------------------------|---------|
| **Sex**          |                                   |         |                                   |         |
| Female           | reference                         |         |                                   |         |
| Male             | 1.87 (1.83, 1.91)                 | < .0001 | 1.83 (1.79, 1.88)                 | < .0001 |
| **Age**          |                                   |         |                                   |         |
| 0-20             | reference                         |         |                                   |         |
| 21-30            | 0.51 (0.45, 0.57)                 | < .0001 | 0.50 (0.44, 0.56)                 | < .0001 |
| 31-40            | 1.17 (1.05, 1.29)                 | .0029   | 1.06 (0.96, 1.7)                  | .268    |
| 41-50            | 3.30 (2.99, 3.63)                 | < .0001 | 2.70 (2.45, 2.98)                 | < .0001 |
| 51-60            | 8.30 (7.55, 9.13)                 | < .0001 | 6.16 (5.60, 6.78)                 | < .0001 |
| 61-70            | 18.44 (16.76, 20.28)              | < .0001 | 12.46 (11.33, 13.73)              | < .0001 |
| 71-80            | 29.30 (26.60, 32.28)              | < .0001 | 19.08 (17.32, 21.06)              | < .0001 |
| 81+              | 31.01 (28.03, 34.31)              | < .0001 | 20.98 (18.96, 23.27)              | < .0001 |
| **Underlying health condition** |          |         |                                   |         |
| Yes              | 4.36 (4.26, 4.46)                 | < .0001 | 2.20 (2.15, 2.26)                 | < .0001 |
| No               | reference                         |         |                                   |         |

Note: Underlying health condition=Yes indicates patients with diabetes, COPD, asthma, immunosuppression, hypertension, CKD, cardiovascular disease, obesity, or other diseases

Note: Some patients have comorbidities

OR: Odds ratio