A survival analysis of COVID-19 in the Mexican population

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Abstract

Background. At present, the Americas region contributes to the largest number of cases of COVID-19 worldwide. In this area, Mexico is in third place respecting deaths (20,781 total deaths), rate that may be explained by the high proportion of the population over 50 years and the rate of chronic diseases. The aim of the present work was estimate the risk factors associated with the death rate, considering the time between symptoms onset and the death occurrence, in the Mexican population.

Methods. Information of all the confirmed cases for COVID-19 reported on the public dataset released by the Epidemiological Surveillance System for Viral Respiratory Diseases of the Mexican Ministry of Health was analyzed. Kapplan-Meier curves were plotted, and a Cox proportional hazard model was constructed.

Results. The analysis included 16,752 registries of confirmed cases of COVID-19 with mean age 46.55±15.55 years; 58.02% (n=9719) men and 9.37% (n=1,569) died. Men (H.R. 1.21, p<0.01, 95% C.I. 1.09-1.35), older age (H.R. 8.24, p<0.01, 95% C.I. 4.22-16.10), CKD (H.R. 1.85, p<0.01, 95% C.I. 1.51-2.25), pneumonia (H.R. 2.07, p<0.01, 95% C.I. 1.81-2.38), hospitalization and ICU admissions (H.R. 5.86, p<0.01, 95% C.I. 4.81-7.14, and H.R. 1.32, p<0.01, 95% C.I. 1.12-1.55, respectively), intubation (H.R. 2.93, p<0.01, 95% C.I. 2.50-3.45) and health care in public health services (more than twice the risk, p<0.01), were independent factors increasing the risk of death due to COVID-19.

Conclusions. The risk of dying at any time during follow-up was especially higher in men, individuals at the older age groups, with chronic kidney disease and people hospitalized in the public health services.

Background

The pandemic caused by the novel coronavirus, SARS-CoV–2, has become one of the biggest health challenges faced worldwide. With almost 9 million confirmed cases and more than 465 thousand deaths to June 22nd, 2020 (1), this pandemic of COVID–19 had turned into one of the public health problems with a meaningful impact in the history of humanity.

By the third week of June, the Americas region contributes to the largest number of cases worldwide. The United States was the country with the highest number of total confirmed COVID–19 cases (2,241,178). Was followed by Brazil (1,067,579 cases), Perú (251,338 cases), Chile (242,355 cases) and Mexico (175,202 cases). Talking about deaths, Mexico stands in third place (20,781 total deaths) (1).

It had been reported that the COVID–19 is commonly presented in an asymptomatic form, frequently improving with the time and without special medical care. A significant proportion of COVID–19 cases develop pneumonia and acute severe respiratory failure (2, 3). These cases commonly require hospitalization, intensive care unit admission, and intubation (4).

Older age, the presence of comorbidities, particularly hypertension, diabetes, obesity, and smoking, are the factors increasing the risk of severe presentation of the disease (5). Notwithstanding, the characteristics of the COVID–19 may vary depending on the demographic and epidemiological profiles of each country. In Mexico's specific case, with 27% of the population over 50 years(6) and a high rate of chronic diseases(7), the risk of fatal complications may be increased.

Assessing the instantaneous rate of death at any time during follow-up for the specific risk factors is crucial to determine the appropriateness of the mitigation strategies and to set up priorities to control the COVID–19 epidemic. This is especially so for countries that are in the present moment focusing their efforts on fighting the pandemic; this is the case of Mexico.

Methods

The aim of the present analysis was to estimate the risk factors associated with the death rate, considering the time between symptoms onset and the death occurrence, in the Mexican population.

Design and settings

Data of the suspected cases of viral respiratory disease reported by the Epidemiological Surveillance System for Viral Respiratory Diseases of the Mexican Ministry of Health (Secretaría de Salud, S. S.) were taken for the present analysis(8). The database included all positive, negative and suspected cases to COVID–19 registered by 475 viral respiratory disease monitoring units (USMER) and by the medical units that attended the cases.

For every individual, information on sex, age, nationality, residence place, migratory status, comorbidities (hypertension, diabetes, obesity, cardiovascular disease, chronic obstructive pulmonary disease (COPD), asthma, chronic kidney disease (CKD), immunosuppression, or other diseases reported by the individual), smoking and pregnancy, was recorded. Regarding the COVID–19 event, type of medical unit of the first contact (S. S. and private services), management received (either hospitalization or outpatient), and dates of COVID–19 symptoms development, admission to hospitalization, and death were recorded. Information on the development of pneumonia, admission to intensive care units (ICU) or intubation were also registered. Data on the evolution during the stay in the medical units were no released for public use.

For the present analysis, all the confirmed cases for COVID–19 registered until April 28th, 2020, were used. Eleven registers reporting the death on the same day of the start of symptoms were eliminated from the analysis. With the date of onset of symptoms before the report of the first case of COVID–19 in Mexico (February 27th, 2020), seven registers were eliminated from the survival analysis.

Variables

The variable time was constructed considering the days from the presentation of symptoms to death (failure). For individuals who did not die, April 28th was established as the date of failure.

Age, sex, comorbidities, pregnancy, immune-suppression, smoking, days from the presentation of symptoms to hospitalization and death, and from admission to health care unit to death, development of pneumonia, hospitalization and ICU admissions, intubation, and the type of health service, were used for the present analysis.

For the survival analysis and the Cox proportional hazard model, sex, morbidity (yes or no for each disease), pneumonia, hospitalization, ICU and intubation were included in a dichotomic way. The variable health services was composed of 5 categories: IMSS, ISSSTE, SS, Other Public Services, and Private Services. For the age, four categories were created <25 years, 25–49 years, 50–74 years, and ≥75 years.

Statistical analysis

Continuous variables are described using means and standard deviations (±SD), and categorical variables are expressed as number and percentage (%). Comparisons between individuals who died vs. those who did not were estimated through the t-Student test for continuous variables and $\chi 2$ for categorical variables. The Kaplan-Meier method was used to plotted the survival curves that were compared by the log-rank and Cox test. The restricted mean survival time and its dispersion measures were calculated. Cox´s Proportional Hazards Model was fitted with the outcome variable and the covariables of interest. All analyses were performed with the statistical package software STATA 14.

Results

The analysis included 16,752 registries of confirmed cases of COVID–19. The mean age of the individuals was 46.55±15.55 years, 58.02% (n = 9719) were men, and 9.37% (n = 1,569) died.

When comparing individuals who died vs those who did not, the former were older (59.42±14.29) and mainly men (67.94%), ($p<0.001$). Prevalence of CKD in people who died (6.86%) was larger in comparison to those who did not die ($p<0.001$). In individuals who survived, the proportion without comorbidities was higher ($p<0.001$). The period from the onset of symptoms to admission in hospitalization was similar between both groups (4.27 ± 3.43, $p = 0.7302$). The period from the onset of symptoms to death and admission to death was 10.15±5.75 and 5.86±5.12 days, respectively. Among the people who died, 75.33% (n = 1,182) developed pneumonia, 90.25% (1,416) was hospitalized, 18.61% (n = 292) was admitted to the ICU and 23.96% (n = 376) needed intubation. These proportions were higher in comparison to individuals who did not die ($p<0.001$). In the group of those who died, 42.65% received health care from IMSS, while in the surviving group, 47.94% received health care from S. S. services (Table 1).

Table 1. General characteristics by outcome

	Total	Dead	No Dead	p value
	n = 16,752	n= 1,569	n = 15,183	
Age, years	46.55 ± 15.55	59.42 ± 14.29	45.22 ± 15.06	0.0000
Sex (men)	9,719 (58.02)	1,066 (67.94)	8,653 (56.99)	0.0001
Comorbidities				
Diabetes	3,064 (18.44)	266 (17.12)	2,798 (18.58)	0.1581
COPD	421 (2.53)	44 (2.83)	377 (2.5)	0.4353
Asthma	585 (3.52)	51 (3.28)	534 (3.55)	0.5882
Hypertension	3,640 (21.91)	353 (22.72)	3,287 (21.82)	0.4186
Cardiovascular Disease	473 (2.85)	43 (2.77)	430 (2.86)	0.8786
Obesity	3,463 (20.83)	340 (21.86)	3,123 (20.73)	0.2935
Chronic kidney disease	388 (2.34)	107 (6.86)	281 (1.87)	0.0001
Number of Comorbidities	0.72 ± 0.94	0.77 ± 0.95	0.71 ± 0.94	0.0296
No Comorbidities	9,173 (54.76)	417 (26.58)	8,756 (57.67)	0.0001
Pregnancy	99 (0.59)	5 (0.32)	94 (0.62)	0.1385
Immuno-suppression	314 (1.89)	25 (1.61)	289 (1.92)	0.3916
Smoking	1,496 (9)	150 (9.62)	1,346 (8.94)	0.3684
Days Sint-Adm	4.27 ± 3.43	4.29 ± 3.49	4.26 ± 3.42	0.7302
Days Adm-Dead	5.86 ± 5.12	5.86 ± 5.12	—	
Days Sint-Dead	10.15 ± 5.75	10.15 ± 5.75	—	
Pneumonia	4,942 (29.5)	1,182 (75.33)	3,760 (24.76)	0.0001
Hospitalized	6,581 (39.28)	1,416 (90.25)	5,165 (34.02)	0.0001
ICU	720 (4.3)	292 (18.61)	428 (2.82)	0.0001
Intubated	709 (4.23)	376 (23.96)	333 (2.19)	0.0001
Dead	1,569 (9.37)	1,569 (100)	—	
IMSS Services	6,262 (37.57)	667 (42.65)	5,595 (37.04)	0.0001
ISSSTE Services	905 (5.43)	124 (7.93)	781 (5.17)	0.0001
SSA Services	7,896 (47.37)	655 (41.88)	7,241 (47.94)	0.0001
Other Public Services	684 (4.1)	87 (5.56)	597 (3.95)	0.0022

Private Services	922 (5.53)	31 (1.98)	891 (5.9)	0.0001

In the survival analysis, a total of 16,734 registers and 1,558 deaths were included. The total analysis time at risk and under observation was 315,773 days. The Kaplan-Meier survival plots for the prognostic factors that resulted statistically significant in the Log-rank and the Cox tests are shown in Figure 1. It can be seen that individuals who developed pneumonia, those with previous diagnosis of CKD and those who were admitted to hospitalization, after 20 days of hospitalization have a statistically lower probability of survival of about 30%, compared to individuals who did not present these characteristics. People who were admitted to the ICU, after 20 days of hospitalization, have a statistically lower probability of survival of approximately 40%, compared to individuals who did not enter this unit. Finally, individuals who needed intubation, after 20 days of hospitalization have a statistically lower probability of survival just about 50%, compared to individuals who were not intubated.

The results of the multivariate Cox proportional hazards regression model can be seen in Table 2. The difference in overall death risk between the two groups was significant ($x^2 = 62.59$, df = 13, $p<0.001$). At any time during follow-up, men were 1.21 times likely to die compared with women. Age increases the risk of dying, and that risk was significantly high in older individuals, who had 8.24 times the risk of dying compared with the youngest age group. People with CKD were 1.85 times likely to die compared with people without this disease. Twice as many individuals who developed pneumonia had died compared to individuals who did not develop this complication. At any time during the follow-up, people admitted to hospitalization and ICU were 5.86 and 1.32 times as likely to die compared with people who were not admitted to those units ($p<0.001$, 95% C. I. 4.81–7.14, and $p<0.001$, 95% C. I. 1.12–1.55, respectively). People who needed intubation were 2.93 times as likely to die compared with individuals who did not require intubation. People receiving health care from IMSS services had 5.64 times the risk of dying compared to people who received health care in private services.

Table 2. Hazard ratio for the fatal outcome in the multivariate Cox proportional hazards regression model.

	Hazard Ratio	Std. Err.	z	P>z	95% C.I.	
Sex (men)	1.21	0.06	3.53	0.000	1.09	1.35
Age (<25 years, reference)						
25-49 y	2.32	0.79	2.49	0.013	1.20	4.50
50-74 y	4.49	1.51	4.46	0.000	2.32	8.67
75 + y	8.24	2.82	6.17	0.000	4.22	16.10
Chronic kidney disease	1.85	0.19	6.04	0.000	1.51	2.25
Pneumonia	2.07	0.15	10.40	0.000	1.81	2.38
Hospitalisation	5.86	0.59	17.53	0.000	4.81	7.14
ICU	1.32	0.11	3.28	0.001	1.12	1.55
Intubation	2.93	0.24	13.14	0.000	2.50	3.45
Health Services (Private, reference)						
IMSS Services	5.64	1.06	9.21	0.000	3.90	8.14
ISSSTE Services	2.98	0.60	5.39	0.000	2.00	4.43
SS Services	3.47	0.64	6.71	0.000	2.41	4.98
Other Public Services	3.23	0.68	5.59	0.000	2.14	4.87

Discussion

The results of our analysis, with Kaplan-Meier survival method and multivariate Cox proportional hazards regression model, were that being a man, older age, CKD, development of pneumonia, hospitalization and ICU admissions, intubation and health care in public health services, are independent risk factors increasing the risk of death due to COVID−19.

Recent reports showed similar results. Men are twice more likely than women to die from COVID−19 (9, 10) and age older than 50 years increases the risk of fatal complications for this disease (11, 12). ICU admission and intubation is an indicator of high-level severity of the disease, both demonstrating an increased risk of death (13). In our analysis, intubation represents a notable risk factor for death as it increased 2.93 times the risk of death.

The mean time from the onset symptoms to death (10.15±5.75 days) was different from that reported in other studies suggesting that death occurs between 14 and 21 days after the onset of symptoms (14). In the present the time between the onset of symptoms until seeking care was similar between people who died and those who survived (p = 0.7302). It can be hypothesized that people with a high risk of severe COVID–19, e.g. with comorbidities, arrived in a critical state to the health services.

A high proportion (58%) of people who did not die from COVID–19 neither had comorbidities. The high prevalence of chronic diseases in both, individuals who died and those who did not, reflects the epidemiological context of Mexico (7) but also the impact of chronic disease in the COVID–19 presentation and severity. This data allows us to hypothesize that the presence of chronic diseases not only increases the risk of complicated disease but even the risk of acquiring the novel coronavirus. A possible explanation is that chronic inflammation, negative effects on immunomodulation and metabolic stress that characterized systemic diseases decrease the ability to react against external agents; in this case, SARS-CoV–2 (15–18).

In our analysis CKD, a common comorbidity of diabetes(19) and hypertension(20), increased 1.85 times the risk of death in comparison to people without this disease. Cheng et al. (21) reported that 13.1% of the people admitted to hospitalization in China had kidney failure. This prevalence is significantly larger than the 2.34% we found in the Mexican population diagnosed with COVID–19. Besides, in the Chinese study, the mortality rate due to CDK (33%) was larger than in our population. While in China, kidney disease was diagnosed at the hospital admission by laboratory tests, in Mexico, the diagnosis was registered on a self-reported basis. Thus, the prevalence and mortality due to this cause may be underestimated in Mexico. The Kaplan-Meier curves in the Chinese study also demonstrated that individuals with kidney disease had a significantly higher risk of in-hospital death. A similar pattern can be observed in the present study. It has been suggested that infection with SARS-CoV–2 may bind renal epithelial cells, injure these cells, and subsequently disrupt the whole body fluid, acid-base, and electrolyte homeostasis, thus increasing the failure in those with preexisting CKD and accelerating the death (22, 23).

A relevant finding of our analysis is that the crude lethality rate of 9.4% is above the 5.3 initially reported in Hubei, China (24), and 6.05% in the United States. However, it is below the 11.76% in Spain, 13.98% in Italy, 14.37% in the United Kingdom and 19.35% in France (25). Such discrepancies can be explained by the way the COVID–19 cases are confirmed and deaths registered. In the majority of countries, only in-hospital deaths are registered, and in countries like Mexico, in the absence of symptoms tests are not used in large quantities (26).

Finally, according to our results, different health service providers may have an essential role in lethality. Public providers reported a larger risk of death in comparison with private ones. Risk of death was the largest for IMSS health care provider (H. R. 5.64) followed by SS services (H. R. 3.47). It is especially important to note that SS and IMSS are the institutions that have received the most cases of COVID–19 in this epidemic, both of uninsured and insured population, hence, having a high probability of over saturation.

Some limitations must be taken into account when analyzing the present results. First, the dataset does not include clinical variables related to the evolution of the COVID–19 which could have been useful in adjusting the model. Second, given that the disease continues and will remain active for an undefined period, it would be desirable to have followed the cohort for a longer time, so that all the probable outcomes associated with the pandemic were observed. The database contains information of all deaths that were confirmed as positive cases of COVID–19. Nevertheless, there is a high percentage of deaths classified as atypical pneumonia and not confirmed as cases of COVID–19, which may underestimate the case fatality rate for this disease.

Despite those above, the present paper contributes to understanding the dynamics of the pandemic in the Mexican context. We highlight risk factors for death that have been little studied, especially the presence of CKD and data regarding the health system that reflects the social inequality in Mexico.

Conclusions

Being a man, older age, CKD, development of pneumonia, hospitalization and ICU admissions, intubation and health care in public health services, are independent risk factors increasing the risk of death due to COVID–19.

Given the likelihood of a second wave of COVID–19, the population at higher risk of fatal outcomes need to be the focus of the mitigation campaigns. In parallel, strengthen public health campaigns aimed at reducing the prevalence of obesity, diabetes, hypertension, and their comorbidities, that are possibly making Mexican population more susceptible to COVID–19 and may cause a rapid progression to severe states of disease and death.

List Of Abbreviations

CKD - Chronic kidney disease

COPD - Chronic obstructive pulmonary disease

COVID–19 - Coronavirus disease 2019

ICU - Intensive care units

IMSS—Mexican Institute of Social Security

ISSSTE—Institute of Social Security and Services of the State Workers

SARS-CoV–2 - Severe acute respiratory syndrome coronavirus 2

SS—Mexican ministry of Health

Declarations

Ethics approval and consent to participate

The use of this public dataset did not need ethical approval

Consent for publication

Not applicable.

Availability of data and materials

The dataset analysed during the current study is available in the Mexican Ministry of Health repository, https://www.gob.mx/salud/documentos/datos-abiertos-152127

Competing interests

The authors declare no competing interests.

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Authors' contributions

All authors gave final approval of the version to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work were appropriately investigated and resolved.

Guillermo Salinas-Escudero: Conceptualization, Methodology, Data curation, Formal analysis, Supervision of the paper writing.

María Fernanda Carrillo-Vega: Conceptualization, Methodology, Writing-Original draft and final manuscript.

Víctor Granados-García: Supervision of the paper writing, Writing - Review & Editing.

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Figures

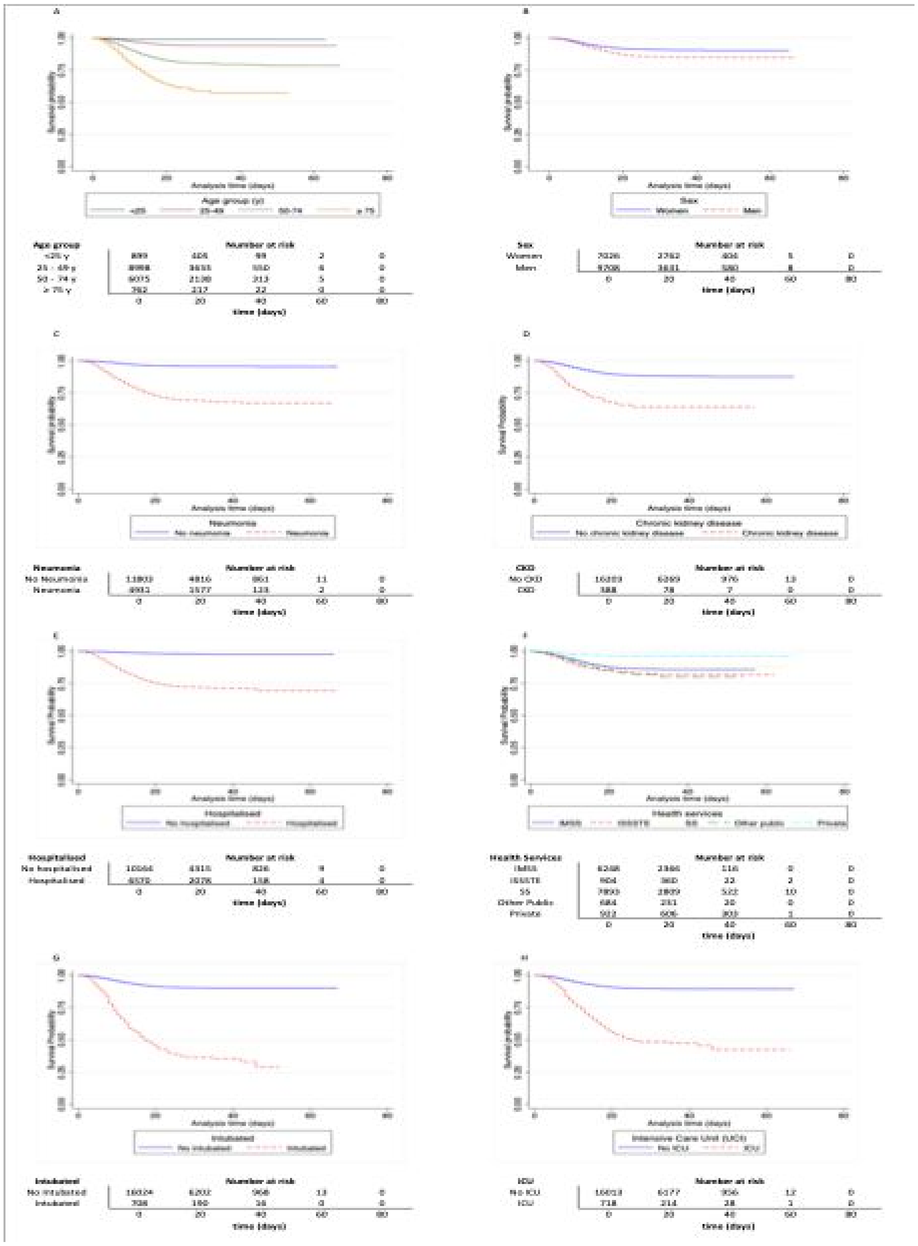

Figure 1

Kaplan-Meier survival plots for different prognostic factors.