Comorbilidad preexistente, el mayor factor de riesgo de mal pronóstico de COVID-19 en la población Mexicana

Pre-existing comorbidity, the highest risk factor for poor prognosis of COVID-19 among the Mexican population

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Resumen

La pandemia de la enfermedad por coronavirus 2019 (COVID-19) representa un desafío para la salud pública y un alto riesgo para los pacientes con comorbilidad preexistente. Al 20 de julio de 2020, la Tasa de Casos Fatales fue de 11.30% y la Tasa de Mortalidad fue de 31.28 muertes por

100,000 habitantes. En México, la prevalencia de obesidad, diabetes mellitus e hipertensión entre la población adulta mexicana es de 30%, 9.2% y 40%, respectivamente. El objetivo de esta investigación fue identificar los factores de riesgo asociados a ocho comorbilidades y su dependencia de la edad para la muerte por COVID-19.

Método: Este estudio utilizó el conjunto de datos publicado el 20 de julio de 2020 por la Dirección General de Epidemiología de la Secretaría de Salud de México. A partir de este conjunto de datos, se analizaron 130.896 casos positivos de COVID-19, donde 35.483 (27,107%) pacientes tenían una comorbilidad y 95.413 (72,892%) pacientes no tenían comorbilidad médica. Los análisis estadísticos incluyen la tasa de letalidad, la estimación de la razón de probabilidades y su intervalo de confianza del 95%.

Resultados: La Tasa de Casos Fatales más altas fue 14.382% para EPOC (Enfermedad Pulmonar Obstructiva Crónica), 10.266% para ERC (Enfermedad Renal Crónica), 10.126% para diabetes y 8.954% para hipertensión. La tasa de riesgo para obesidad fue del 3,535%. Además, se detectó un mayor riesgo para los pacientes con EPOC, diabetes y ERC, lo que resultó en una OR de 4,443 (IC del 95%: 3,404-5,799), 3,283 (IC del 95%: 3,018-3,570) y 3,016 (IC del 95%: 2.248-4.047), respectivamente.

Conclusión: Este estudio corrobora que el mayor riesgo de enfermedad grave y muerte causada por COVID-19 entre la población mexicana son las comorbilidades preexistentes. Los resultados muestran que EPOC, ERC, diabetes, hipertensión y enfermedades cardiovasculares aumentan el riesgo de muerte para pacientes mayores a 54 años. El grupo de edad más vulnerable es el de mayor a 65 años.

Palabras clave: tasa de letalidad; comorbilidad; coronavirus; COVID-19; riesgo de muerte; pandemia; salud pública; tasa de mortalidad; SARS-CoV-2; salud; diabetes; hipertensión; enfermedades cardiovasculares; edad de riesgo

Abstract

The coronavirus disease 2019 (COVID-19) pandemic represents a challenge for public health and a high risk for patients with pre-existing comorbidity. As of July 20, 2020, the Case Fatality Rate (CFR) was 11.30% and the Mortality Rate (MR) was 31.28 deaths per 100,000 population. In Mexico, the prevalence of obesity, diabetes mellitus, and hypertension among the adult Mexican population is 30%, 9.2%, and 40%, respectively. The objective of this research was to identify the

risk factors associated with eight comorbidities and their dependency on age for death caused by COVID-19.

Method: This study used the dataset published on July 20, 2020, by the General Directorate of Epidemiology of the Ministry of Health of Mexico. From this dataset, we analysed 130,896 positive COVID-19 cases, where 35,483 (27.107%) patients had one comorbidity, and 95,413 (72.892%) patients had not medical comorbidity. Statistical analyses include the Case Fatality Rate (CFR), the estimation of the Odds Ratio (OR), and its 95% Confidence Interval (CI).

Results: The highest CFR was 14.382% for COPD, 10.266% for CKD, 10.126% for diabetes, and 8.954% for hypertension. The obesity CFR was 3.535%. Moreover, we detected a higher risk for patients with COPD, diabetes, and CKD, resulting in OR of 4.443 (95% CI: 3.404-5.799), 3.283 (95% CI: 3.018-3.570), and 3.016 (95% CI: 2.248-4.047), respectively.

Conclusion: This study corroborates that the highest risk for severe disease and death caused by COVID-19 among the Mexican population are pre-existing comorbidities. Findings show that COPD, CKD, diabetes, hypertension, and cardiovascular disease increase the risk of death for patients older than 54 years. The most vulnerable age group is older than 65 years.

Keywords: case fatality rate; comorbidity; coronavirus; COVID-19; death risk; pandemic; public health; mortality rate; SARS-CoV-2; Health; diabetes; hypertension; cardiovascular diseases; age of risk

Introduction

Since the new type of Coronavirus Disease 2019 (COVID-19) appeared in Wuhan, China, the number of patients with a confirmed infection continues growing around the world. On July 20, 2020, the World Health Organization (WHO) reported a total of 14,349,855 confirmed cases in the world.

According to the General Directorate of Epidemiology of the Ministry of Health of Mexico, on July 20, 2020, the number of confirmed cases of COVID-19 were 349,396 and 39,485 deaths associated with COVID-19, which means a Mortality Rate (MR) of 31.28 deaths per 100,000 population and a Case Fatality Rate (CFR) of 11.30%. Based on the rapid spread and high MR of COVID-19, it is necessary to identify the risk factors affecting the progression of the COVID-19 among the Mexican population.

Previous studies show that COVID-19 patients and pre-existing comorbidity are at higher risk for poor prognosis (Suleyman, *et al*., 2020), (Thombs, *et al.*, 2007), (Wang, He, *et al.*,2020), (Wang, Li, *et al.*, 2020), (Wu & McGoogan, 2020), identifying as major risk factors diabetes (Holman, *et al.*, 2020), (Klonoff & Umpierrez, 2020), (Miyazawa, 2020), hypertension (Miyazawa, 2020), (Singh, *et al.*, 2020), (Zuin, *et al.*, 2020), obesity (Dietz & Santos-Burgoa, 2020), (Miyazawa, 2020), (Ryan, *et al.*, 2020), Chronic Kidney Disease (CKD) (Henry & Lippi, 2020), (Yamada, *et al.*, 2020), cardiovascular disease (Bansal, 2020), (Wang, He, *et al.*,2020), Chronic Obstructive Pulmonary Disease (COPD) (Wang, Li, *et al.*, 2020). Among the Mexican population, obesity (DiBonaventura, *et al.*, 2017), (Hernández-Garduño, 2020), diabetes (Rojas-Martínez, *et al.*, 2018) and hypertension (Campos-Nonato, *et al.*, 2018) are the major risk factors (Carrillo-Vega, *et al.*, 2020), (Parra-Bracamonte, *et al.*, 2020).

From this point, the purpose of this study was to identify the risk factors associated with eight comorbidities and their dependency on age for death caused by COVID-19 among the Mexican population.

Method

The General Directorate of Epidemiology of the Ministry of Health of Mexico published on July 20, 2020, a dataset with the epidemiological study of a suspected case of viral respiratory disease where the patients were able to answer yes, no, or unknown in each question (Secretaria de Salud, 2020).

The dataset provides demographic data including age, gender, state, and information about the following comorbidities and conditions: asthma, cardiovascular disease, CKD, COPD, contact with a person who had a positive test result for COVID-19, diabetes, immunosuppression, hypertension, obesity, other comorbidities, pregnancy, presence of pneumonia, and smoking.

Also, the dataset provides healthcare data, such as type of patient (ambulatory or hospitalized), hospitalized in the intensive care unit (yes, no, or unknown), intubated (yes, no, or unknown), and the laboratory test result of COVID-19 by Polymerase Chain Reaction (positive, false, or pending result). Moreover, the dataset includes the following dates: 1) when the patient developed symptoms associated with COVID-19, 2) when the patient was hospitalized, and 3) when the patient died. We created the variable death (yes or no) based on the date of death.

Selection of Variables

It is important to highlight that the prevalence of obesity in Mexico affects over 30% of the adult population (DiBonaventura, *et al.*, 2017), which is strongly associated with cardiovascular disease and type 2 diabetes mellitus. Another relevant data is that Mexico appears in the top ten countries with diabetes mellitus patients. According to (Rojas-Martínez, 2018), the prevalence of diabetes mellitus in Mexico affects over 9.2% of the population. This comorbidity is strongly associated with CKD. Finally, but not less important, hypertension was diagnosed in 40% of the adult population (Campos-Nonato, *et al.*, 2016).

For the purpose of this study, we included records of positive COVID-19 patients with no medical comorbidities and with one of the following comorbidities: 1) asthma, 2) cardiovascular disease, 3) CKD, 4) diabetes, 5) COPD, 6) immunosuppression, 7) hypertension, and 8) obesity. Age was classified into five groups: 0-14, 15-24, 25-54, 55-64, and older than 65 years for the rest of this analysis.

Statistical Analysis of Data

A descriptive analysis of data was performed using Microsoft Excel ®. Discrete variables were examined to identify the risk factor for death between COVID-19 patients with and without comorbidity. Statistical analyses include the CFR, the estimation of the OR, and its 95% CI, using SPSS © (Statistical Package for the Social Sciences) software.

Results

The analysis included a total of 130,896 positive COVID-19 cases, where 35,483 (27.107%) patients had one comorbidity, and 95,413 (72.892%) patients had not medical comorbidity. Obesity was the most prevalent comorbidity (11.128%), followed by hypertension (7.397%) and diabetes (5.296%) in the entire group.

The age group with the highest percentage of positive cases was adult patients between 25 and 54 years (72.551%), where hypertension was the most frequent comorbidity (15.599%), followed by diabetes (12.565%) and obesity (8.931%). Among patients older than 65 years, 4674 (47.188%) had one comorbidity; of 4674 patients with one comorbidity, hypertension was the most frequent comorbidity (24.796%), followed by diabetes (12.479%) and obesity (4.886%).

The COVID-19 Case Fatality Rate among patients with one comorbidity was 6.484% and 2.635% for patients without comorbidity. By age group, the patients between 55 and 64 years, and older than 65 years had the highest CFR 8.518% and 19.485%, respectively. Patients older than 65 years had the highest CFR among patients without comorbidity (17.874%) and with comorbidity (21.287%).

Of the total number of COVID-19 patients with one comorbidity, the highest CFR was 14.382% for COPD, 10.266% for CKD, 10.126% for diabetes, and 8.954% for hypertension. The obesity CFR was 3.535%. Records revealed that CKD patients between 25 and 54 years and 55 and 64 years with COVID-19 infection had the highest CFR of 7.668% and 15.384%, respectively.

Table 1. Clinical characteristics of patients with COVID-19 by age group in Mexico.

Characteristics	Positive cases n = 130896				CFR	OR (95% CI)
Age group (0 – 14)	Death n = 16	%	Total n = 2207	%	0.724	1.232 (0.591 – 2.568)
Age group (15 – 24)	Death n = 28	%	Total n = 9284	%	0.301	1.557 (0.861 – 2.817)
Age group (25 – 54)	Death n = 1604	%	Total n = 94967	%	1.689	1.826 (1.682 – 1.984)
Without comorbidity	885	55.17	71529	75.32	1.237	1.102 (1.003 – 1.211)
Diabetes	208	12.97	3789	3.99	5.490	5.394 (4.649 – 6.257)
COPD	11	0.69	159	0.17	6.918	6.265 (3.389 – 11.58)
Asthma	18	1.12	1726	1.82	1.043	0.885 (0.553 – 1.407)
Immunosuppression	10	0.62	317	0.33	3.155	2.741 (1.458 – 5.155)
Hypertension	146	9.10	4876	5.13	2.994	2.733 (2.301 – 3.246)
Cardiovascular disease	5	0.31	301	0.32	1.661	1.417 (0.585 – 3.435)
Obesity	296	18.45	11944	12.58	2.478	2.362 (2.081 – 2.680)
CKD	25	1.56	326	0.34	7.669	7.05 (4.676 – 10.631)
Age group (55 – 64)	Death n = 1238	%	Total n = 14533	%	8.518	1.945 (1.765 – 2.144)
Without comorbidity	664	53.63	8677	59.71	7.652	1.339 (1.199 – 1.496)
Diabetes	212	17.12	1826	12.56	11.610	2.018 (1.728 – 2.357)
COPD	12	0.97	107	0.74	11.214	1.795 (0.985 – 3.280)
Asthma	7	0.57	141	0.97	4.965	0.738 (0.344 – 1.581)
Immunosuppression	4	0.32	80	0.55	5.000	0.744 (0.272 – 2.037)
Hypertension	206	16.64	2267	15.60	9.087	1.489 (1.275 – 1.739)
Cardiovascular disease	3	0.24	85	0.58	3.529	0.517 (0.163 – 1.637)
Obesity	122	9.85	1298	8.93	9.399	1.514 (1.246 – 1.841)
CKD	8	0.65	52	0.36	15.385	2.582 (1.213 – 5.496)
Age group (65 +)	Death n = 1604	%	Total n = 9905	%	19.485	2.322 (2.135 – 2.524)
Without comorbidity	935	48.45	5231	52.81	17.874	1.156 (1.052 – 1.270)
Diabetes	281	14.56	1236	12.48	22.734	1.541 (1.337 – 1.777)

COPD	41	2.12	174	1.76	23.563	1.550 (1.089 – 2.207)
Asthma	12	0.62	65	0.66	18.461	1.131 (0.603 – 2.120)
Immunosuppression	15	0.78	66	0.67	22.727	1.472 (0.826 – 2.622)
Hypertension	512	26.53	2456	24.80	20.846	1.416 (1.267 – 1.582)
Cardiovascular disease	26	1.35	124	1.25	20.967	1.329 (0.860 – 2.053)
Obesity	92	4.77	484	4.89	19.008	1.180 (0.935 – 1.488)
CKD	16	0.83	69	0.70	23.188	1.511 (0.862 – 2.648)
Age group (All)	Death n = 4816	%	Total n = 130896	%	3.679	1.950 (1.857 – 2.047)
Without comorbidity	2515	52.22	95413	72.89	2.635	0.390 (0.368 – 0.414)
Diabetes	702	14.58	6932	5.30	10.126	3.283 (3.018 – 3.570)
COPD	64	1.33	445	0.34	14.382	4.443 (3.404 – 5.799)
Asthma	38	0.79	2241	1.71	1.695	0.447 (0.324 – 0.617)
Immunosuppression	31	0.64	564	0.43	5.496	1.526 (1.061 – 2.194)
Hypertension	867	18.00	9682	7.40	8.954	2.921 (2.705 – 3.153)
Cardiovascular disease	34	0.71	566	0.43	6.007	1.678 (1.185 – 2.376)
Obesity	515	10.69	14566	11.13	3.535	0.955 (0.870 – 1.048)
CKD	50	1.04	487	0.37	10.266	3.016 (2.248 – 4.047)

COPD: Chronic Obstructive Pulmonary Disease; **CKD:** Chronic Kidney Disease;

CFR: Case Fatality Rate; Odds Ratio and 95% Confidence Interval.

In the analysis focused on the risk of death among COVID-19 patients with one comorbidity, we found a higher risk of death for patients older than 65 years followed by 55 to 64 years and 25 to 54 years with an OR of 2.322 (95% CI: 2.135 – 2.524), 1.945 (95% CI: 1.765 – 2.144) and 1.826 (95% CI: 1.682 – 1.984), respectively. In contrast, we detected a lower risk for patients without comorbidity with an OR of 0.390 (95% CI: 0.368-0.414).

Considering each comorbidity, we detected a higher risk for patients with COPD, diabetes, and CKD, resulting in OR of 4.443 (95% CI: 3.404-5.799), 3.283 (95% CI: 3.018-3.570), and 3.016 (95% CI: 2.248-4.047), respectively. By stratifying the patients by age groups, we detected a higher risk for patients in the age group of 25-54 years with an OR of 7.05 (95% CI: 4.676-10.631) for CKD, 6.265 (95% CI: 3.389-11.58) for COPD, and 5.394 (95% CI: 4.649-6.257) for diabetes.

Discussion

The present study provides a more specific analysis of the CFR of eight comorbidities and COVID-19 infection as it did not consider deaths from all causes (combination between two or more comorbidities) among patients during or after COVID-19 treatment. The existence of a national database of suspected cases of COVID-19 (Secretaría de Salud, 2020) allowed identifying the magnitude of each comorbidity and its dependency on age as a risk factor for death among the Mexican population. The results are congruent with previous studies (Carrillo-Vega, 2020), (Parra-Bracamonte, *et al.*, 2020), demonstrating that obesity, hypertension, and diabetes were the comorbidities more prevalent among the Mexican population.

At this time, the increasing number of cases and expansion of COVID-19 in Mexico is causing widespread concern among the population. Despite all the efforts, the number of deaths due to COVID-19 is still considerable, especially among patients with COPD, CKD, diabetes, and hypertension. In New York City, a study had reported risk factors for severe COVID-19 disease in 210 CKD patients, demonstrating that among patients with CKD, severe cases had a higher risk of mortality and intubation (Yamada, *et al.*, 2020) among each age group, requiring more attention from patients and medical units. Patients with obesity between 25 and 64 years have a higher risk of death in our study.

We were surprised to find that asthma has a lower risk of death with an OR 0.447 (95% CI: 0.324-0.617) in the entire group, corroborating previous results (Bousquet, *et al.*, 2020), (Carli, *et al.*, 2020), (Suleyman, *et al.*, 2020). This result has similitude to the cases reported in China, where asthma had not prevalence as a risk factor for mortality (Wang, Pawankar, *et al.*, 2020). As a consequence, it is necessary to further studies on the antiviral and immunomodulatory activities of asthma medications (Johnston, 2020) to take advantage of its benefits in finding a cheap treatment for the Mexican population.

The risk of death from COVID-19 and one comorbidity increased with age, as demonstrated by (Carrillo, *et al.*, 2020), (Parra-Bracamonte, *et al.*, 2020), (Suleyman, *et al.*, 2020), (Thombs, *et al.*, 2007), (Wu & McGoogan, 2020). Age group older than 65 years has a higher risk of death with a CFR of 19.485% and OR of 2.322 (95% CI: 2.135-2.524). On the other hand, the study

corroborates that young patients (Wu & McGoogan, 2002) had a lower risk of death. Younger age groups, 0-14 years and 15-24 years had a CFR of 0.724% and 0.301%, and OR of 1.232(95% CI: 0.591-2.568) and 1.557 (95% CI: 0.864-2.817), respectively. In Mexico, the 25-54 age group has a higher number of positive patients, which requires a specific study to understand the national context and employment situation.

This study considers official data, which implies assuming different risks or difficulties in interpreting the data contained in the databases. It should be remembered that the complexity that exists with the application, registration, monitoring and control of the pandemic makes it difficult to have a statistical precision than other research could have. In any case, the decision to assess the official data shows important in is against health policies, medical services, and a whole health culture itself than exceeds the scope of this work, but which could be identified.

Conclusion

Our findings also provide a degree of clarity in areas where previous studies have not been in agreement, including the risk factor for mortality among patients with CKD and COPD, and the low risk of death of patients with asthma and COVID-19. It is unclear the future for positive COVID-19 patients, in the following months, in Mexico; however, we can say with certainty that the pre-existing comorbidities among Mexican population represent a high risk of death, which could increase the public health and social expenditures. With this and previous studies, it is clear that the best strategy to reduce deaths is the prevention, in terms of, reduce comorbidities among the Mexican population.

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