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Short Report

Obesity is the comorbidity more strongly associated for Covid-19 in Mexico. A case-control study

Eduardo Hernández-Garduño

Dirección de Administración y Desarrollo de Personal. Instituto de Seguridad Social del Estado de México y Municipios (ISSEMyM), Toluca Estado de México, Mexico

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A B S T R A C T

Some comorbidities are associated with severe coronavirus disease (Covid-19) but it is unclear whether some increase susceptibility to Covid-19. In this case-control Mexican study we found that obesity represents the strongest predictor for Covid-19 followed by diabetes and hypertension in both sexes and chronic renal failure in females only. Active smoking was associated with decreased odds of Covid-19. These findings indicate that these comorbidities are not only associated with severity of disease but also predispose for getting Covid-19. Future research is needed to establish the mechanisms involved in each comorbidity and the apparent “protective” effect of cigarette smoking.

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Introduction

Early reports have identified obesity among other comorbidities such as diabetes, hypertension, coronary artery disease, and heart failure, as risk factors associated with severe outcomes in hospitalized patients with Covid-19 [1–4]. However, only one cross sectional study so far has determined risk factors for Covid-19 in the general population and found obesity and chronic kidney disease (CKD) to be predictors with no statistically significant association for other chronic conditions [5]. This study included patients with two or more comorbidities which may have underestimated the strength of association between obesity and CKD with Covid-19 because the correlation of comorbidities, for example diabetes with obesity, or with hypertension, and the assumption of little or no multicollinearity in the multivariable logistic regression analysis would not be met which may explain why other chronic conditions were not associated with Covid-19 in that study. In this study we determined comorbidities associated with increased risk for Covid-19 in a population based-study of Mexicans reporting one comorbidity as of May 15, 2020. The present study updates a previous study (Unpublished results as of May 7, 2020) with a bigger sample size of patients.

Methods

This study used the publicly available Covid-19 data base of the Mexican Ministry of Health through the “Dirección General de Epidemiología” website [6] from which information was obtained of all patients assessed for Covid-19 as of May 15, of 2020. Variables in the data base include non-nominal ID (randomly assigned), age, gender, current smoker, history of contact with Covid-19, type of patient: ambulatory vs hospitalized and whether or not the patient was hospitalized in the intensive care unit (ICU) or had been intubated (tracheal intubation for mechanical ventilation). Information also included answers “yes, no, unknown” or no answer when questioned about the presence/absence of the following conditions and comorbidities: pregnancy in women, diabetes, hypertension, cardiovascular disease, chronic obstructive pulmonary disease (COPD), asthma, obesity, chronic renal failure (CRF) and immunosuppression conditions without specification of each. The presence of pneumonia was also recorded but was considered part of the clinical picture of Covid-19 rather than comorbidity. Only patients who answered “yes or no” to all the above questions were included in the analysis. Patients who did not respond or with missing information were excluded. Some patients presented with multiple comorbidities that may be correlated, for example diabetes and obesity, and the assumption of little or no

* Corresponding author at: Departamento de Seguridad e Higiene ISSEMyM, Av. Constituyentes #703, Col. Barrio de la Merced, Toluca de Lerdo, Estado de México, CP 50080, Mexico.
E-mail address: epidemiologist.researcher@gmail.com

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multicollinearity of logistic regression analysis would not be met. To separate the effect of two or more comorbidities and determine the independent effect of each on Covid-19, the analysis was limited to patients reporting only one comorbidity. Laboratory test results of Covid-19 PCR test were reported as “positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)”, “negative for SARS-CoV-2” or “pending result”. Cases were defined as those with a positive test regardless of symptoms according to World Health Organization case definition [7]. Controls were those with negative test.

In univariable analysis, proportions for categorical variables were compared using the χ² test. Median age of both groups was compared with the Mann–Whitney U test. To determine comorbidities associated with Covid-19, odds ratios (OR) and 95% confidence intervals were estimated using multivariable logistic regression with the backward elimination procedure. Indicator variables for each comorbidity were included in the model with absence of each as the reference group. Statistical analyses were performed using SAS (Statistical Analysis System, Cary, NC, USA) version 9.4 software.

Table 1
Characteristics of cases and controls of the whole sample as of May 15, 2020. Univariable and multivariate logistic regression analyses for increasing risk of Covid-19.

| Age group (years) | Median age (IQR) in years, range | Contact with COVID-19 | Smoking history | Cardiovascular disease | COPD | Asthma | Non-immunesuppression | Chronic renal failure | Non-chronic renal failure | Pregnant | Tracheally intubated | In ICU | Non-ICU | Death | Alive |
|------------------|----------------------------------|-----------------------|----------------|------------------------|------|--------|-----------------------|----------------------|------------------------|----------|---------------------|--------|---------|--------|-------|
|                   |                                  | Yes                   | No              | Yes                    | No   | Yes    | No                   | Yes                  | No                     | Yes       | Yes                  | Yes    | Yes     | Yes    | Yes   |
| 0–29              | 48 (38–59), 0–113                | 3141 (43.3)           | 4109 (56.7)     | 1191 (9.7)             | 11083 (90.3) | 4219 (34.3)       | 8084 (65.7)          | 4717 (38.4)          | 7552 (61.6)           | 2596 (21.1)       | 9680 (78.9)          | 2887 (23.5)       | 9389 (76.5)       | 212 (1.7) | 12061 (98.3) |
| 30–52             | 42 (32–54), 0–102                | 6492 (52.8)           | 5083 (41.3)     | 7221 (58.7)            | 5807 (41.3) | 4720 (38.4)       | 4720 (38.4)          | 5539 (45.0)          | 6765 (55.0)           | 7221 (50.7)       | 12061 (98.3)          | 212 (1.7)         | 12061 (98.3)       | 212 (1.7) | 12061 (98.3) |
| 53+               | 8084 (4717)                      | 16371 (51.3)          | 15852 (48.7)    | 16371 (51.3)           | 15852 (48.7) | 16371 (51.3)      | 16371 (51.3)         | 16371 (51.3)         | 16371 (51.3)           | 16371 (51.3)       | 16371 (51.3)          | 16371 (51.3)      | 16371 (51.3)       | 16371 (51.3) | 16371 (51.3) |
| Total             |                                  | 16371 (51.3)          | 15852 (48.7)    | 16371 (51.3)           | 15852 (48.7) | 16371 (51.3)      | 16371 (51.3)         | 16371 (51.3)         | 16371 (51.3)           | 16371 (51.3)       | 16371 (51.3)          | 16371 (51.3)      | 16371 (51.3)       | 16371 (51.3) | 16371 (51.3) |

SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; IQR: interquartile range; COPD: chronic obstructive pulmonary disease; ICU: intensive care unit; NS: not selected by the backward elimination procedure in the multivariable logistic regression analysis with a significance level set at 0.2; NI: not included in the multivariate analysis; Covid-19: coronavirus disease.

a Unadjusted odds ratio and 95% confidence interval.

b Differences between cases and controls. Totals may not add up due to missing data.

c Adjusted odds ratio and 95% confidence interval.
Table 2
Characteristics of females as of May 15, 2020. Univariate and multivariate logistic regression analyses for increasing risk of Covid-19.

|                        | Cases SARS-CoV-2 positive | Controls SARS-CoV-2 Negative | Total | uOR (95% CI) a | p b | aOR (95% CI) c | p  
|------------------------|---------------------------|-----------------------------|-------|----------------|-----|----------------|-----
| Age group (years)      | n = 5083                  | n = 10,679                   | n = 15,852 |                |     |                |     
| 0-29                   | 48 (37–58), 0–113         | 42 (32–52), 0–102            | 44 (34–54), 0–113 | <.0001 |     |                |     
| Contact with COVID-19  | Yes                       | 1465                        | 50.6 | 3452           | 49.8 | 4952           | 50.0 | 0.96 (0.88–1.05) | 0.45 | 1.42 (1.13–1.8) | 0.0025 | 
| Smoking history        | Yes                       | 289                         | 5.7  | 891            | 8.3  | 1180           | 7.5  | 0.68 (0.58–0.76) | <.0001 | 0.49 (0.31–0.78) | <.0023 | 
| Chronic renal failure  | No                        | 4788                        | 94.3 | 9868           | 91.7 | 14,656         | 92.5 | 1              |       |                  |       | 
| Hypertension           | No                        | 1414                        | 27.8 | 1292           | 12.0 | 2,706          | 17.1 | 2.82 (2.59–3.07) | <.0001 | 1.56 (1.25–1.93) | <.0001 | 
| Cardiovascular disease | Yes                       | 1967                        | 38.8 | 3,582          | 33.3 | 5,549          | 35.0 | 1.26 (1.18–1.36) | <.0001 | 5.55 (4.09–7.51) | <.0001 | 
| Chronic renal failure  | No                        | 3107                        | 61.2 | 7,181          | 66.7 | 10,288         | 65.0 | 1              |       |                  |       | 
| Immunosuppression      | Yes                       | 914                         | 18.0 | 1,309          | 12.2 | 2,223          | 14.0 | 1.58 (1.44–1.73) | <.0001 | 3.91 (2.98–5.29) | <.0001 | 
| Non-immunosuppression  | No                        | 4,161                       | 82.0 | 9,446          | 87.8 | 13,607         | 86.0 | 1              |       |                  |       | 
| Cardiac disease        | Yes                       | 78                          | 1.5  | 280            | 2.6  | 358            | 2.3  | 0.58 (0.45–0.75) | <.0001 | NS               |       | 
| Non-cardiac disease    | No                        | 4,999                       | 98.5 | 10,476         | 97.4 | 15,475         | 97.7 | 1              |       |                  |       | 
| Asthma                 | No-COPD                   | 68                          | 1.3  | 222            | 2.1  | 290            | 1.8  | 0.64 (0.49–0.84) | 0.0015 | NS               |       | 
| Chronic renal failure  | No                        | 5,009                       | 98.7 | 10,536         | 97.9 | 15,545         | 98.2 | 1              |       |                  |       | 
| Non-immunosuppression  | Non-immunosuppression     | 350                         | 6.9  | 1,488          | 13.8 | 1,838          | 11.6 | 0.46 (0.40–0.52) | <.0001 | 3.25 (3.36–4.48) | <.0001 | 
| Chronic renal failure  | No                        | 4,725                       | 93.1 | 9,276          | 86.2 | 14,001         | 88.4 | 1              |       |                  |       | 
| Non-immunosuppression  | Yes                       | 95                          | 1.9  | 402            | 3.7  | 497            | 3.1  | 0.49 (0.39–0.61) | <.0001 | NS               |       | 
| Chronic renal failure  | No                        | 4,977                       | 98.1 | 10,353         | 96.3 | 15,330         | 96.9 | 1              |       |                  |       | 
| Diabetes               | No                        | 64                          | 1.3  | 136            | 1.3  | 200            | 1.3  | 0.99 (0.74–1.34) | 0.99  | 2.25 (1.69–3.01) | 0.0011 | 
| Non-immunosuppression  | Yes                       | 5010                        | 98.7 | 10,626         | 98.7 | 15,636         | 98.7 | 1              |       |                  |       | 
| Non-immunosuppression  | No                        | 63                          | 1.2  | 174            | 1.6  | 237            | 1.5  | 0.76 (0.57–1.02) | 0.07  | NS               |       | 
| Death                  | No                        | 5005                        | 98.8 | 10,566         | 98.4 | 15,572         | 98.5 | 1              |       |                  |       | 
| Hypertension           | No                        | 176                         | 9.4  | 155            | 7.6  | 331            | 8.4  | 1.25 (1.0–1.57)  | 0.04  | NS               |       | 
| Non-immunosuppression  | No                        | 1,705                       | 90.6 | 1,890          | 92.4 | 3,595          | 91.6 | 1              |       |                  |       | 
| Death                  | No                        | 424                         | 8.3  | 220            | 2.0  | 644            | 4.1  | 4.3 (3.69–5.15)  | <.0001 | 2.25 (1.69–3.01) | <.0001 | 

SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; IQR: interquartile range; COPD: chronic obstructive pulmonary disease; ICU: intensive care unit; NS: not selected by the backward elimination procedure in the multivariable logistic regression analysis with a significance level set at 0.2; NI: not included in the multivariate analysis; Covid-19-coronavirus disease.

a Unadjusted odds ratio and 95% confidence interval.
b Differences between cases and controls. Totals may not add up due to missing data.
c Adjusted odds ratio and 95% confidence interval.

Results

A total 32,583 patients (12,304 cases and 20,279 controls) were identified with one comorbidity.

Cases were older than controls, median age in years (interquartile range) of 48 (38–59) vs 42 (32–54) respectively, and more likely to be: males (58.7 vs 47% females) and hospitalized (45 vs 23% ambulatory) or to have had pneumonia (34.3 vs 15.2%) diabetes (21.1 vs 13.3%), hypertension (23.5 vs 21.3%), obesity (38.4 vs 32.4%) admitted to the ICU (10.4 vs 8.2%) intubated (10.5 vs 6.5%) respectively. Cases were also more likely to have died (12.2 vs 2.7%) respectively. Univariable analysis showed controls more likely to have had a history of: contact with Covid-19, current smoking, cardiovascular, COPD, asthma or immunosuppressed conditions, all p-values<0.0001. Table 1. After controlling by variables associated with Covid-19 in univariate analysis, the following comorbidities remained statistically significant in the multivariable analysis by sex: obesity (females:aOR = 5.55, males-aOR = 4.72), diabetes (females-aOR = 3.91, males-aOR = 3.50), hypertension (females-aOR = 3.25, males-aOR = 2.70) and chronic renal failure (females-aOR = 2.25). Active smoking was associated with decreased odds of Covid-19 (females-aOR = 0.49, males-aOR = 0.64) as was the group of immunosuppressed conditions in males (aOR = 0.50), Tables 2 and 3.
Table 3
Characteristics of males as of May 15, 2020. Univariate and multivariate logistic regression analyses for increasing risk of Covid-19.

|                      | Cases SARS-CoV-2 positive | Controls SARS-CoV-2 Negative | Total | uOR (95% CI) \* | p | aOR (95% CI) \* | p |
|----------------------|---------------------------|-----------------------------|-------|-----------------|---|-----------------|---|
| Median age (IQR) in years, range | 49 (39–59), 0–103 | 43 (32–55), 0–99 | 46 (34–57), 0–103 | .0001 | 1 | 1 | 1 |
| Age group (years)    |                           |                             |       |                 |   |                 |   |
| 0–29                                                             | 573                        | 79                          | 1808  | 19.0            | 2381 | 14.2            | 1 |
| 30–52                                                            | 3772                       | 52.2                        | 4886  | 51.4            | 8658 | 51.7            | .0001 |
| 53 +                                                             | 2876                       | 39.8                        | 2816  | 29.6            | 5692 | 34.0            | .0001 |
| Hospitalized outpatient | 3656                      | 50.6                        | 2586  | 27.2            | 6242 | 37.3            | .0001 |
| Contact with COVID-19                                           | 3565                       | 49.4                        | 6924  | 72.8            | 10489| 62.7            | 1 |
| Smoking history                                                  |                           |                             |       |                 |   |                 |   |
| Yes                                                               | 1676                       | 39.1                        | 3008  | 48.3            | 4684 | 44.6            | .0001 |
| No                                                                | 2609                       | 60.9                        | 3214  | 51.7            | 5823 | 55.4            | 1 |
| Pneumonia                                                         | 902                        | 12.5                        | 1508  | 15.9            | 2410 | 14.4            | .0001 |
| No                                                                | 6295                       | 87.5                        | 7993  | 84.1            | 14288| 85.6            | 1 |
| Obesity                                                           | 2805                       | 38.8                        | 1798  | 18.9            | 4603 | 27.5            | .0001 |
| No                                                                | 4416                       | 61.2                        | 7711  | 81.1            | 12127| 72.5            | 1 |
| Diabetes                                                          | 2750                       | 38.2                        | 2978  | 31.3            | 5728 | 34.3            | .0001 |
| No                                                                | 4445                       | 61.8                        | 6525  | 68.7            | 10970| 65.7            | 1 |
| Hypertension                                                     | 1682                       | 23.4                        | 1392  | 14.7            | 3074 | 18.4            | .0001 |
| No                                                                | 5519                       | 76.6                        | 8103  | 85.3            | 13622| 81.6            | 1 |
| Cardiovascular disease                                           | 1729                       | 24.0                        | 2207  | 23.2            | 3936 | 23.6            | .0001 |
| No                                                                | 5469                       | 76.0                        | 7293  | 76.8            | 12762| 76.4            | 1 |
| COPD                                                              | 134                        | 1.9                         | 303   | 3.2             | 437  | 2.6             | .0001 |
| No                                                                | 7062                       | 98.1                        | 9196  | 96.8            | 16258| 97.4            | 1 |
| Asthma                                                            | 126                        | 1.8                         | 269   | 2.8             | 395  | 2.4             | .0001 |
| No                                                                | 7072                       | 98.2                        | 9231  | 97.2            | 16303| 97.6            | 1 |
| Non-asthma                                                       | 273                        | 3.8                         | 951   | 10.0            | 1224 | 7.3             | .0001 |
| Immunosuppression                                                | 6992                       | 96.2                        | 8547  | 90.0            | 15469| 92.7            | 1 |
| Non-immunosuppression                                            | 118                        | 1.6                         | 375   | 4.0             | 493  | 3.0             | .0001 |
| Chronic renal failure                                            | 103                        | 1.4                         | 173   | 1.8             | 276  | 1.7             | .0001 |
| Non-chronic renal failure                                        | 7093                       | 98.6                        | 9328  | 98.2            | 16421| 98.3            | 1 |
| Tracheally intubated                                             | 429                        | 11.7                        | 168   | 6.5             | 597  | 9.6             | .0001 |
| Non-intubated                                                    | 3225                       | 88.3                        | 2415  | 93.5            | 5640 | 90.4            | 1 |
| In ICU                                                            | 399                        | 10.9                        | 226   | 8.7             | 625  | 10.0            | .0001 |
| Non-ICU                                                          | 3255                       | 89.1                        | 2357  | 91.3            | 5612 | 90.0            | 1 |
| Death                                                             | 1078                       | 14.9                        | 324   | 3.4             | 1402 | 8.4             | .0001 |
| alive                                                            | 6143                       | 85.1                        | 9166  | 96.6            | 15329| 91.6            | 1 |

SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; IQR: interquartile range; COPD: chronic obstructive pulmonary disease; ICU: intensive care unit; NS: not selected by the backward elimination procedure in the multivariable logistic regression analysis with a significance level set at 0.2; aOR: not included in the multivariate analysis; Covid-19: coronavirus disease.

\* Unadjusted odds ratio and 95% confidence interval.
\[ Differences between cases and controls. Totals may not add up due to missing data.
\[ Adjusted odds ratio and 95% confidence interval.

Discussion

The findings of this update and the previous analysis of data of May 7, 2020 (Unpublished results) indicate that obesity is the strongest predictor for Covid-19 among Mexicans followed by diabetes and hypertension. CRF was a risk factor in females only. This risk increase for Covid-19 is alarming. The higher odds ratios in females than males suggest that females with obesity, diabetes and hypertension are more susceptible for Covid-19.

These findings indicate that common comorbidities associated with severe Covid-19 outcomes also predispose this disease. Among the potential mechanisms for the association include the higher susceptibility of the obese to respiratory viral infections including influenza A [8] and increased duration of virus shedding [9] which may also be the case for SARS-CoV-2. Obesity is a state of low-grade chronic inflammation that can contribute to the onset of dyslipidemia, insulin resistance and diabetes and can modify innate and adaptive immune responses, resulting in a less responsive immune system to vaccinations, antivirals and antimicrobial drugs and more vulnerable to infections [10]. Further research is needed to confirm whether obesity represents the strongest predictor for getting Covid-19 in other populations and settings.

Potential implicated mechanisms on the association between diabetes and Covid-19 include chronic inflammation, increased coagulation activity, immune response impairment, and potential direct pancreatic damage by SARS-CoV-2 [11]. Diabetics are particularly more susceptible to bacterial, mycotic, parasitic and viral infections [12].

SARS-CoV-2 binds to angiotensin converting enzyme (ACE) 2 in the lung to enter cells [13,14], this cell surface diminution of ACE2...
may contribute to widespread inflammation observed with Covid-19. Angiotensin-converting enzyme inhibitors are recommended treatments for cardiovascular diseases, hypertension and chronic kidney disease and have been postulated to impact SARS-CoV-2 host-cell interactions [15]. Unfortunately information regarding patients undergoing treatment for these conditions is unavailable in the data base and needs to be explored to establish whether medication types predispose Covid-19 in Mexican patients with these comorbidities and determine the potential mechanisms involved. The increased risk of Covid-19 among females with CRF also warrants further investigation as does the mechanisms involved.

Asthma was associated with Covid-19 but only in the analysis of the whole sample. The lack of association in either sex may be related with the relative small sample size. The relationship between asthma and respiratory virus infection has been recognized [16] but is not well understood. A larger sample size would yield more data as to the population of asthmatics and the mechanism of Covid-19 susceptibility.

The decreased odds of Covid-19 among immunosuppressed males may be influenced by relatively small sample size and needs confirmation in future studies as well as identifying the specific immunosuppression illnesses associated with Covid-19.

The lower smoking prevalence in patients with Covid-19 compared with controls found in this study is consistent with preliminary estimates showing the same trend [17]. Active smoking remained statistically significant in the multivariable analysis which is consistent with recent findings [5]. Nicotine has been proposed as a therapeutic option for Covid-19 [18]. Further research is needed to confirm the “protective” effect of active smoking on Covid-19.

Pregnancy was not associated with Covid-19 in the multivariate analysis restricted to women. Table 2.

This study has some limitations namely that patients presenting symptoms of Covid-19 would be more investigated for comorbidities and/or tested selecting bias affecting the estimates. Unfortunately, body mass index (BMI), symptoms, laboratory results and treatment of comorbidities was not available in the data base. Future studies including this information will more accurately determine the association of comorbidities with Covid-19.

This study is one of the first Mexican studies on Covid-19 indicating that obesity is the comorbidity more strongly associated with Covid-19. In 2016 the prevalence of overweight and obesity combined was 72.5% in Mexican adults aged 20 years or older [19] and was declared public health emergency by the government of Mexico. Diabetes, hypertension and CRF were also risk factors of disease.

This work compares a previous analysis of the database extracted may 7, 2020 (Unpublished results) and the results of both analyses are similar. Both indicate that comorbidities frequently found in patients with severe Covid-19 are also risk factors for the disease. Future studies will determine the potential mechanisms behind the association between these predisposing comorbidities with Covid-19.

Patients with comorbidities found to be associated with this disease should take extreme preventive measures and physicians should be aware of such associations when assessing patients with Covid-19 symptoms and take appropriate precautions.

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**Ethics statement**

Ethics approval was not required as the study was based on de-identified routine daily data publicly available.

**Conflict of interest**

The author has no conflicts of interest relevant to this article.

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