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Short Report

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

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ABSTRACT

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 pre-

vious study (Unpublished results as of May 7, 2020) with a bigger sample size of patients.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

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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 χ^2 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. 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
	n = 12,304	%	n = 20,279	%	n = 32,583	%				
Males	7221	58.7	9510	46.9	16,731	51.3	1.6 (1.5–1.7)	<.0001	1.48 (1.31–1.68)	<.0001
Females	5083	41.3	10,769	53.1	15,852	48.7				
Median age (IQR) in years, range	48 (38–59), 0–113		42 (32–54), 0–102		45 (34–56), 0–113			<.0001		
Age group (years)										
0–29	1092	8.9	3885	19.2	4977	15.3	1		1	
30–52	6492	52.8	10,894	53.7	17,386	53.4	1.25 (1.22–1.27)	<.0001	2.49 (1.97–3.15)	<.0001
53 +	4720	38.4	5500	27.1	10,220	31.4	1.45 (1.42–1.48)	<.0001	2.59 (2.04–3.28)	<.0001
Hospitalized	5539	45.0	4636	22.9	10,175	31.2	2.76 (2.63–2.9)	<.0001	1.48 (1.31–1.68)	<.0001
Outpatient	6765	55.0	15,643	77.1	22,408	68.8	1		1	
Contact with COVID-19										
Yes	3141	43.3	6491	49.3	9632	47.2	0.79 (0.74–0.83)	<.0001	1.29 (1.11–1.5)	0.0008
No	4109	56.7	6666	50.7	10,775	52.8	1		1	
Smoking history										
Yes	1191	9.7	2399	11.8	3590	11.0	0.8 (0.74–0.86)	<.0001	0.63 (0.51–0.77)	<.0001
No	11,083	90.3	17,861	88.2	28,944	89.0	1		1	
Pneumonia	4219	34.3	3090	15.2	7309	22.4	2.9 (2.8–3.1)	<.0001	1.46 (1.27–1.67)	<.0001
No-pneumonia	8084	65.7	17,187	84.8	25,271	77.6	1		1	
Obesity	4717	38.4	6560	32.4	11,277	34.7	1.31 (1.25–1.37)	<.0001	6.92 (5.54–8.65)	<.0001
Non-obesity	7552	61.6	13,706	67.6	21,258	65.3	1		1	
Diabetes	2596	21.1	2701	13.3	5297	16.3	1.74 (1.64–1.85)	<.0001	5.02 (4.02–6.25)	<.0001
No-diabetes	9680	78.9	17,549	86.7	27,229	83.7	1		1	
Hypertension	2887	23.5	4306	21.3	7193	22.1	1.14 (1.08–1.2)	<.0001	3.99 (3.17–5.01)	<.0001
No-hypertension	9389	76.5	15,953	78.7	25,342	77.9	1		1	
Cardiovascular disease	212	1.7	583	2.9	795	2.4	0.59 (0.51–0.7)	<.0001	1.8 (1.21–2.69)	0.0039
No-cardiovascular diseases	12,061	98.3	19,672	97.1	31,733	97.6	1		1	
COPD	194	1.6	491	2.4	685	2.1	0.65 (0.55–0.76)	<.0001	NS	
No-COPD	12,081	98.4	19,767	97.6	31,848	97.9	1		1	
Asthma	623	5.1	2439	12.0	3062	9.4	0.39 (0.36–0.43)	<.0001	1.73 (1.2–2.49)	0.0036
Non-asthma	11,647	94.9	17,823	88.0	29,470	90.6	1		1	
Immunosuppression	213	1.7	777	3.8	990	3.0	0.44 (0.38–0.52)	<.0001	NS	
Non-immunesuppression	12,057	98.3	19,471	96.2	31,528	97.0	1		1	
Chronic renal failure	167	1.4	309	1.5	476	1.5	0.89 (0.74–1.08)	0.23	2.66 (1.73–4.11)	<.0001
No-chronic renal failure	12,103	98.6	19,954	98.5	32,057	98.5	1		1	
Pregnant	63	1.2	174	1.6	237	1.5	0.76 (0.57–1.02)	0.07	NI	
No-pregnant	5005	98.8	10,567	98.4	15,572	98.5	1		1	
Tracheally intubated	580	10.5	301	6.5	881	8.7	1.68 (1.46–1.95)	<.0001	NS	
Non-intubated	4956	89.5	4327	93.5	9283	91.3	1		1	
In ICU	575	10.4	381	8.2	956	9.4	1.29 (1.13–1.48)	0.0002	NS	
Non-ICU	4960	89.6	4247	91.8	9207	90.6	1		1	
Death	1502	12.2	544	2.7	2046	6.3	5.0 (4.56–5.58)	<.0001	2.52 (2.12–3)	<.0001
Alive	10,802	87.8	19,735	97.3	30,537	93.7	1		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; 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
	n = 5083	%	n = 10,769	%	n = 15,852	%				
Median age (IQR) in years, range	48 (37–58), 0–113		42 (32–52), 0–102		44 (34–54), 0–113			<.0001		
Age group (years)										
0–29	519	10.2	2077	19.3	2596	16.4	1		1	
30–52	2720	53.5	6008	55.8	8728	55.1	1.16 (1.13–1.19)	<.0001	2.05 (1.46–2.89)	<.0001
53 +	1844	36.3	2684	24.9	4528	28.6	1.34 (1.30–1.39)	<.0001	2.55 (1.80–3.58)	<.0001
Hospitalized	1883	37.0	2050	19.0	3933	24.8	2.50 (2.32–2.69)	<.0001	NS	
Outpatient	3200	63.0	8719	81.0	11,919	75.2	1			
Contact with COVID-19										
Yes	1465	49.4	3483	50.2	4948	50.0	0.96 (0.88–1.05)	0.45	1.42 (1.13–1.8)	0.0025
No	1500	50.6	3452	49.8	4952	50.0	1		1	
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
No	4788	94.3	9868	91.7	14,656	92.5	1		1	
Pneumonia	1414	27.8	1292	12.0	2706	17.1	2.82 (2.59–3.07)	<.0001	1.56 (1.25–1.93)	<.0001
No-pneumonia	3668	72.2	9476	88.0	13,144	82.9	1		1	
Obesity	1967	38.8	3582	33.3	5549	35.0	1.26 (1.18–1.36)	<.0001	5.55 (4.09–7.51)	<.0001
Non-obesity	3107	61.2	7181	66.7	10,288	65.0	1		1	
Diabetes	914	18.0	1309	12.2	2223	14.0	1.58 (1.44–1.73)	<.0001	3.91 (2.98–5.29)	<.0001
No-diabetes	4161	82.0	9446	87.8	13,607	86.0	1		1	
Hypertension	1158	22.8	2099	19.5	3257	20.6	1.21 (1.12–1.32)	<.0001	3.25 (3.36–4.48)	<.0001
No-hypertension	3920	77.2	8660	80.5	12,580	79.4	1		1	
Cardiovascular disease	78	1.5	280	2.6	358	2.3	0.58 (0.45–0.75)	<.0001	NS	
No-cardiovascular diseases	4999	98.5	10,476	97.4	15,475	97.7	1		1	
COPD	68	1.3	222	2.1	290	1.8	0.64 (0.49–0.84)	0.0015	NS	
No-COPD	5009	98.7	10,536	97.9	15,545	98.2	1		1	
Asthma	350	6.9	1488	13.8	1838	11.6	0.46 (0.40–0.52)	<.0001	NS	
Non-asthma	4725	93.1	9276	86.2	14,001	88.4	1		1	
Immunosuppression	95	1.9	402	3.7	497	3.1	0.49 (0.39–0.61)	<.0001	NS	
Non-immunosuppression	4977	98.1	10,353	96.3	15,330	96.9	1		1	
Chronic renal failure	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
No-chronic renal failure	5010	98.7	10,626	98.7	15,636	98.7	1		1	
Pregnant	63	1.2	174	1.6	237	1.5	0.76 (0.57–1.02)	0.07	-NS	
No-pregnant	5005	98.8	10,567	98.4	15,572	98.5	1		1	
Tracheally intubated	151	8.0	133	6.5	284	7.2	1.25 (0.98–1.59)	0.06	NS	
Non-intubated	1731	92.0	1912	93.5	3643	92.8	1		1	
In ICU	176	9.4	155	7.6	331	8.4	1.25 (1.0–1.57)	0.04	NS	
Non-ICU	1705	90.6	1890	92.4	3595	91.6	1		1	
Death	424	8.3	220	2.0	644	4.1	4.3 (3.69–5.15)	<.0001	2.25 (1.69–3.01)	<.0001
Alive	4659	91.7	10,549	98.0	15,208	95.9	1		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; 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 anal-

ysis 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) ^a	p ^b	aOR (95% CI) ^c	p
	n = 7221	%	n = 9510	%	n = 16,731	%				
Median age (IQR) in years, range	49 (39–59), 0–103		43 (32–55), 0–99		46 (34–57), 0–103			<.0001		
Age group (years)										
0–29	573	7.9	1808	19.0	2381	14.2	1	1		
30–52	3772	52.2	4886	51.4	8658	51.7	1.34 (1.30–1.38)	<.0001	2.87 (2.07–3.98)	<.0001
53 +	2876	39.8	2816	29.6	5692	34.0	1.53 (1.48–1.58)	<.0001	2.59 (1.87–3.60)	<.0001
hospitalized	3656	50.6	2586	27.2	6242	37.3	2.74 (2.57–2.92)	<.0001	NS	
outpatient	3565	49.4	6924	72.8	10,489	62.7	1			
Contact with COVID-19										
Yes	1676	39.1	3008	48.3	4684	44.6	0.68 (0.63–0.74)	<.0001	1.21 (1.00–1.47)	0.0466
No	2609	60.9	3214	51.7	5823	55.4	1		1	
Smoking history										
Yes	902	12.5	1508	15.9	2410	14.4	0.75 (0.69–0.83)	<.0001	0.64 (0.51–0.81)	0.0002
No	6295	87.5	7993	84.1	14,288	85.6	1		1	
Pneumonia	2805	38.8	1798	18.9	4603	27.5	2.72 (2.54–2.92)	<.0001	1.37 (1.15–1.64)	0.0004
no-pneumonia	4416	61.2	7711	81.1	12,127	72.5	1		1	
Obesity	2750	38.2	2978	31.3	5728	34.3	1.35 (1.27–1.44)	<.0001	4.72 (3.69–6.04)	<.0001
non-obesity	4445	61.8	6525	68.7	10,970	65.7	1		1	
Diabetes	1682	23.4	1392	14.7	3074	18.4	1.77 (1.64–1.91)	<.0001	3.50 (2.74–4.46)	<.0001
no-diabetes	5519	76.6	8103	85.3	13,622	81.6	1		1	
Hypertension	1729	24.0	2207	23.2	3936	23.6	1.04 (0.97–1.12)	0.23	2.70 (2.09–3.48)	<.0001
no-hypertension	5469	76.0	7293	76.8	12,762	76.4	1		1	
Cardiovascular disease	134	1.9	303	3.2	437	2.6	0.57 (0.46–0.70)	<.0001	NS	
no-cardiovascular diseases	7062	98.1	9196	96.8	16,258	97.4	1		1	
COPD	126	1.8	269	2.8	395	2.4	0.61 (0.49–0.75)	<.0001	NS	
no-COPD	7072	98.2	9231	97.2	16,303	97.6	1		1	
Asthma	273	3.8	951	10.0	1224	7.3	0.35 (0.30–0.40)	<.0001	NS	
non-asthma	6922	96.2	8547	90.0	15,469	92.7	1		1	
Immunosuppression	118	1.6	375	4.0	493	3.0	0.40 (0.32–0.49)	<.0001	0.50 (0.31–0.82)	0.0065
non-immunesuppression	7080	98.4	9118	96.0	16,198	97.0	1		1	
Chronic renal failure	103	1.4	173	1.8	276	1.7	0.78 (0.61–1.0)	0.0506	NS	
no-chronic renal failure	7093	98.6	9328	98.2	16,421	98.3	1		1	
tracheally intubated	429	11.7	168	6.5	597	9.6	1.91 (1.58–2.30)	<.0001	NS	
non-intubated	3225	88.3	2415	93.5	5640	90.4	1		1	
in ICU	399	10.9	226	8.7	625	10.0	1.28 (1.07–1.52)	0.0049	NS	
non-ICU	3255	89.1	2357	91.3	5612	90.0	1		1	
death	1078	14.9	324	3.4	1402	8.4	4.97 (4.37–5.65)	<.0001	2.68 (2.15–3.34)	<.0001
alive	6143	85.1	9186	96.6	15,329	91.6	1		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; 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.

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 representing selection 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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