The tale of two pandemics: High prevalence of severe obesity among patients with suspected COVID-19

La Historia de dos Pandemias: alta prevalencia de obesidad severa en pacientes con sospecha de COVID-19

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ABSTRACT

Background: Obesity is frequent in Mexico, but its importance for COVID-19 is still under debate. We aimed to describe its frequency in patients with severe COVID-19 in a referral hospital. **Materials and methods:** 167 patients hospitalized for suspicious or confirmed COVID-19, 66.7% male with a median age of 54 (interquartile range 43-63) were classified according to BMI and evaluated for comorbidities, coronavirus-2 polymerase chain reaction test results, and reason for discharge. **Results:** 75.3% of the patients were overweight or obese and 7.8% had grade III obesity. Increasing BMI related to higher probabilities of hyperglycemia (fasting glucose > 100 mg/dL, $p = 0.044$), but other comorbidities were similar among groups. The mortality rate among patients with Grade I obesity was 11%, whereas 33% of patients with either underweight or Grade III obesity died, depicting a U-shaped mortality curve. **Conclusions:** Obesity and its comorbidities are common in hospitalized patients in Mexico. Special efforts must be made to detect them, and further interventions to control the obesity pandemic will also be necessary to improve long-term results.

Key words: Coronavirus disease-19. Severe obesity. Severe acute respiratory syndrome coronavirus 2. Comorbidities.

RESUMEN

Antecedentes: la obesidad severa es frecuente en México, pero su impacto en el COVID-19 es debatida. Buscamos describir su frecuencia en pacientes con COVID-19 severo en un hospital de referencia. **Material y métodos:** 167 pacientes hospitalizados con COVID-19 (sospechoso o confirmado), 66.7% hombres con una mediana de edad de 54 años (rangos intercuartílicos 43-63) se clasificaron de acuerdo al IMC, sus comorbilidades, la prueba de reacción de polimerasa para coronavirus-2 y causa de egreso. **Resultados:** 75.3% tenían sobrepeso u obesidad y 7.8% estaban en obesidad grado III. El aumento de IMC se relacionó con mayor probabilidad de hiperglucemia (glucosa en ayuno > 100 mg/dL, $p=0.044$), otras comorbilidades fueron similares entre grupos. La mortalidad en pacientes con obesidad grado I fue 11% y 33% en peso bajo u obesidad grado III, mostrando una curva con forma de U. **Conclusiones:** La obesidad y sus comorbilidades son comunes en pacientes hospitalizados en México. Se deben hacer esfuerzos especiales por detectarlas y se necesitarán intervenciones sobre la pandemia de obesidad para mejorar resultados a largo plazo.

Palabras clave: COVID-19. Obesidad severa. SARS-CoV-2. Comorbilidades.

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INTRODUCTION

The novel coronavirus disease (COVID)-19 pandemic has uncovered the deficiencies of most health-care systems in the world. The global burden of the disease is still being calculated; however, the future scenarios regarding economy and health are not encouraging¹. On the other hand, the obesity pandemic has been decreasing the healthy life expectancies for over a decade, with only minor advances being made in some societies². Mexico has shown staggering increases in obesity in the past few years. Currently placed 2nd only to the USA in terms of the prevalence of obesity in adults, the last national health survey (ENSANUT 2018) revealed that 75.2% of the population over 20 years of age has some degree of overweight and obesity (73% of men and 76.8% of women) and around 3% of the population is classified as having severe (Grade III) obesity with a body mass index (BMI) of 40 kg/m² or more. The survey also showed that the increase by year of survey, gender, and affiliation, and the differences cannot be explained by socioeconomic status³. The combination of these two pandemics has been a major concern for health-care providers since obesity has been documented as a risk factor for complications after the infection by the severe acute respiratory syndrome coronavirus (SARS-CoV-19), the causal pathogen of COVID-19. Obesity seems to be the major determinant of complications in patients younger than 60 years old that are apparently healthy⁴. Referral centers are usually dedicated to the attention of complicated diseases that require a multidisciplinary approach. Our hospital is currently a "hybrid referral center," meaning it receives patients with suspicion of COVID-19 but also continues to treat patients with complicated comorbidities. We aimed to determine the frequency of overweight and obesity in the patients hospitalized due to a possible SARS-CoV-19 infection.

MATERIALS AND METHODS

Since the reconversion of the hospital from a purely third level referral center to an hybrid hospital,

there have been more than 2720 evaluations in the "Respiratory Triage." Only the patients that fulfill the current definitions of a "suspicious case for COVID-19," with severe manifestations, are admitted to the COVID-19 hospitalization building. The hospital belongs to the Mexican Institute of Social Security (IMSS), which provides for the care of around 60% of the population. Healthcare is provided at no cost for insured workers and their immediate family members, with funding provided by the Mexican government and monthly payments by the employers and enterprises. The Hospital de Especialidades del Centro Medico Nacional Siglo XXI is a referral center for all specialized medicine, excluding cardiology, oncology, orthopedics, and gynecology.

The respiratory triage is guided by internal medicine and emergency medicine specialists, following the current local guidelines for the definition of a suspected case of SARS-CoV-19:

- Person of any age that presents with two or more of the following signs or symptoms in the past 7 days:
 - Cough
 - Fever
 - Headache
- Plus at least one of the following:
 - Dyspnea (severity)
 - Arthralgia
 - Myalgia
 - Odynophagia
 - Rhinorrhea
 - Conjunctivitis
 - Chest pain.

A confirmed case is a patient that fulfills the criteria for a suspicious case and that has the diagnosis confirmed by the approved laboratories (National Public Health Laboratory Network or the Institute for Epidemiologic Diagnosis and Reference, InDRE), defined in the COVID-19 Mexico, Daily Technical communication, Phase 3, Sunday May 3, 2020, issued by the Mexican Health Secretary⁵.

The patients suspected of COVID-19 are tested according to the sentinel protocol established by the National Health Secretary. There are no rapid tests available in our institution; the tested patients are subjected to nasopharyngeal sampling for SARS-CoV-2 polymerase chain reaction (PCR) tests. The results are processed by a central laboratory and reported by an internet platform. No systematic testing for other respiratory viruses is available at the moment.

Approximately 6% of the patients are referred to hospitalization, whether in the same hospital or their corresponding nearby general hospital. We included the patients that were hospitalized between April 1, 2020, and May 8, 2020, that fulfilled the previous criteria. Patients or their closest family members were invited to participate in the study by signing the appropriate informed consent form. The patients were not subjected to any differential treatment, and they were only asked to provide consent for the evaluation of their medical records (including medical history and laboratory results). The treating physicians were in charge of deciding the appropriate management.

The BMI was calculated using the data from the files for the weight (in kilograms) and height (in meters) using the same scale with stadimeter available in the respiratory triage. If the patients were unconscious or unable to stand in the scale, the data from their previous visit to a doctor's office were used. The formula for BMI was $\text{weight}/(\text{height} \times \text{height})$. The result, expressed in kg/m^2 , was then classified as low weight if it was under $18.5 \text{ kg}/\text{m}^2$, normal if it was between 18.6 and $24.99 \text{ kg}/\text{m}^2$, overweight if 25.0 and 29.99 , Grade I obesity if BMI was 30.0 and 34.9 , Grade II obesity for BMI of 35.0 and 39.9 , and Grade III or severe obesity if BMI was 40.0 or more kg/m^2 .

The patients and family members were guaranteed confidentiality and the right to withdraw their consent, according to the Helsinki protocols. The investigation was approved by the National Investigation Committee from the Mexican Institute of Social Security and deemed to impose no harm or direct benefit to the patients.

The results are expressed in percentages or in medians and interquartile ranges (IQR) due to the

distribution of the variables; for the rest of the analysis, non-parametric tests were performed. $p < 0.05$ was considered to be significant using the results calculated with SPSS v. 21.00.

RESULTS

A total of 167 patients (66.5% male) agreed to participate. We excluded another 52 patients, in which data were not available or did not agree to participate. The median age was 54 (IQR 43-63), and 66.7% were male. In the total group, 70% of the patients were under 60 years old. In total, 57.1% had some form of glucose metabolism disorder (including patients that had a previous history of diabetes pre-diabetes and the patients that had glycated hemoglobin of $> 5.6\%$ at admission or stress induced hyperglycemia, defined as fasting serum glucose of $> 100 \text{ mg}/\text{dL}$ during the first 24 h of hospitalization, with a normal glycated hemoglobin), 46.9% had a previous history of hypertension, 35.4% had been treated for dyslipidemia, 20.8% for heart disease (including ischemia, heart failure, valvulopathy, or arrhythmia), had been diagnosed with 24.4% chronic kidney disease, 23.8% had history of neoplasia, (most of them hematologic malignancies including chronic and acute leukemia, one patient had Stage IV prostate cancer, one had a malignant thymoma, one with hepatocarcinoma and hepatitis C chronic infection, one with renal carcinoma and three had breast cancer), all malignancies were considered to be active at the time of hospitalization and all of them were receiving medical therapy (including chemotherapy) at the onset of the respiratory infection, except for the patient with renal carcinoma who was considered to be cured with surgery, which had been performed 6 months before. In total, 24.5% were or had been smokers, and three patients had undergone bariatric surgery in the past 2 years (one was still in Grade I obesity, one overweight and one had low weight). Many of the patients were not aware of their chronic diseases or the diagnosis was done a few weeks before or during the hospital stay. In total, 18.6% of the patients were detected with elevated glucose during their

Figure 1. Distribution of the patients hospitalized in a referral center for “Suspected COVID-19,” according to their body mass index.

hospitalization, 8% of the patients had been diagnosed with hypertension only in the previous 3 months and 8.7% of the chronic kidney failures were also detected during the hospital stay.

The information regarding these morbidities was recollected from the electronic medical files that included the medical history and direct interrogatory at admission.

PCR test results for SARS-CoV-2 at the time of writing this article were: negative in 20.4%, positive in 39.5%, results pending 19.8%, and not tested 20.4%. These four groups were similar in terms of age, comorbidities, and other evaluated variables.

Only 14.3% of the patients had a normal weight, 10.4% were in the range of low weight, 32.5% were overweight, and 42.9% were in the range of obesity. In figure 1, we can see that the female patients were distributed between the low and obesity Grade II classifications while the Grade III obesity patients were the only male.

Obesity (BMI of 30.0 or more kg/m^2) tended to be more common in patients under 60 years of age. In the group of patients under 60 years of age, 50% had a BMI of 30 mg/kg^2 or more versus the “older

patients” (60 years of age or older), in which 40% of the group had this BMI; however, statistical significance was not achieved ($p = 0.056$).

We can also see in figure 1 that 7.8% of the male patients were classified as having severe obesity (Grade III or a BMI of 40 kg/m^2 or more). The patients with BMI > 25 kg/m^2 (overweight and obesity in any degree) were more likely to have any degree of hyperglycemia (odds ratios [OR] 4.213, confidence intervals [CI] 95% 1.372-12.938, $p = 0.009$) and less likely to have a neoplasia (OR 0.170, CI 95% 0.0046-0.623, $p = 0.005$), but they had similar OR for hypertension, dyslipidemia, lung, kidney, or heart diseases.

The patients with obesity (BMI of 30 kg/m^2 or more) were less likely to have a comorbid neoplasia ($p = 0.034$) and tended to be more likely to have glucose metabolism abnormalities than leaner patients ($p = 0.059$), but no significant difference was found in this analysis. There was also no difference in the OR of having hypertension, dyslipidemia, heart, kidney, or lung disease. The time from diagnosis of comorbidities was similar when we compared to the patients with any degree of obesity (BMI of 30 kg/m^2 or more) against other BMI, except for the time from diagnosis of hyperglycemia (11 years

Table 1. Frequency of deaths over the total discharges in each group according to the body mass index (BMI)

Classification according to BMI	#	Death/ total discharges in this category
Low weight	3	33.3%
Normal	8	37.5%
Overweight	15	20.0%
Grade I obesity	9	11.1%
Grade II obesity	7	14.3%
Grade III obesity	3	33.3%

Figure 2. The frequency of hyperglycemia in each group of body mass index (BMI). The higher the BMI, the higher frequencies of hyperglycemia.

from diagnosis for the patients with BMI < 30 kg/m² and 1 year for the patients with BMI of > 30 kg/m², $p = 0.003$).

When we compared severe obesity versus other BMI, we did find a higher probability of having hyperglycemia in this group, compared to patients with BMI of < 40 kg/m² (OR 1.139, CI 95% 1.016-1.277, $p = 0.044$), we also did not find any other association with this BMI and the OR of having other metabolic comorbidities.

In total, 15% were not considered to have a confirmed comorbidity (hyperglycemia, hypertension, dyslipidemia, heart, lung or kidney disease, or neoplasia).

The number of comorbidities is higher in patients with severe obesity, but there is not a correlation between the number of comorbidities and the

BMI, since all comorbidities may be present even in low BMI. Figure 2 shows that even patients with low BMI had hyperglycemia (25% of the cases), but the patients with severe obesity were affected in 100%.

Finally, at this time, we only have data of discharge in 56.3% of the patients. From the available data, 76.6% of the patients were discharged due to improvement in their conditions and 23.4% died. In the group of patients with a positive PCR for SARS-CoV-2, the mortality rate was 15%. In patients with a negative PCR, the mortality rate was 17.8%. In those that were not tested or had pending test results, 50% died. With the available data, the distribution of discharges by BMI was more favorable for the overweight and Grade I obesity groups, where mortality is lower. The mortality by BMI classification shows an U Shape, with one-third of the patients in

low weight and Grade III obesity dead and the lowest rates in overweight and Grade I obesity.

DISCUSSION

The pandemic caused by SARS-CoV-2 is highlighting many other health-care problems worldwide, many of which have been under debate for decades. Obesity is another pandemic that has been growing relentlessly but has also been underestimated and controversial in many aspects, from the economic, to the socio-cultural and health-care points of view^{6,7}. Each country has faced particular issues regarding the management of COVID-19, given their own characteristics and resources, and Latin America has several problems that undermine the readiness of the countries to face the virus⁸. Mexico and the USA are most affected by the obesity pandemic⁹, with almost 40% of the adult population being classified as obese (BMI > 30 kg/m²) and the numbers rising by 0.95 kg/m² per decade¹⁰. By contrast, trends in BMI have apparently flattened in northwestern Europe and the English-speaking Asia-Pacific regions¹⁰. Some regions report obesity prevalence of 5% or less, while most populations are reaching 10%. Overweight and obesity have been related to several comorbidities, such as the components of metabolic syndrome, cardiovascular disease, cancer, and sleep disorders¹¹. Both obesity and its comorbidities have been related to a significant reduction in life expectancy (from 5 to 10 years depending on the population) and almost 20 years of "healthy" or "active" life expectancy, which can be defined as quality-adjusted life years, years without cardiovascular disease and disability-free years, among others^{12,13}.

It is not surprising then that an aggressive viral pandemic that is increasing death rates among people with these diseases is the cause of concern of countries such as Mexico. In Wuhan, the epicenter of the COVID-19 pandemic, a study by Zhou and collaborators showed that 48% of the patients had comorbidities, the most common were hypertension (30%), diabetes (19%), and coronary heart disease (8%)¹⁴. The previous metabolic and cardiovascular

diseases seemed to have the biggest impact on poor outcomes¹⁵. Europe followed China in the pandemic, with the highest mortality rates in Spain and Italy, bringing obesity to the spotlight. Further research showed that a BMI of 40 kg/m² or more was the strongest predictor for hospitalization (OR 6.2), only after the age of 65 years or more¹⁶. A French group showed that patients with severe obesity were at greater risk of requiring mechanical ventilation¹⁷. Severe obesity has been listed as an independent risk factor for vulnerability or severe illness by the USA Centers for Disease Control and Prevention, but there is still controversy regarding their specific management due to the lack of information on risk of illness for people with extreme forms of obesity¹⁸. The adipose tissue has been shown to have a pro-inflammatory activity that can be harmful to the bronchial tissue¹⁹.

Since our hospital is a third level referral center for specific diseases and access is not available for the open population, we expect to have higher frequencies of comorbidities. The proportion of normal and low BMIs reflect the characteristics of the general population, where less than 25% fall within these ranges; however, we found that there is a large proportion of patients with Grade III obesity (twice the proportion of the general population) and the numbers may be higher considering that 3 patients had undergone bariatric surgery and that the patients with active neoplasias reported weight losses between 5 kg and 20 kg in the last year. The rationale of "hybrid hospitals" in our institution is supported by the fact that patients with complicated comorbidities are the ones that are in the greatest danger of having complications, and such patients are in desperate need of continuous and specialized evaluations. Cancer, dialysis, difficult-to-treat diabetes, or hypertension, HIV, and other diseases cannot defer their treatments until the pandemic resolves. Obesity is clearly an important factor for hospitalization in the COVID-19 area of our hospital, mimicking the results of other series.

Our study is limited by the fact that we included patients that fulfill the diagnostic criteria for "suspicious case," where some of them ended up having a positive PCR and others a negative

confirmatory test, the limited sample size, and the selection bias associated to referral centers. These results may not represent only the cases where there is a clear diagnosis of SARS-CoV-2 infection, but it does reflect the group of high-risk patients that require hospitalization during the pandemic, where the initial clinical evaluation may not be enough to determine if the patient is indeed a positive case or not, but will require interdisciplinary attention. The large percentage of negative patients is also important due to the fact that there were no real clinical differences in the severity of obesity and the presence of comorbidities, their imaging results and baseline laboratory tests were similar, leading to the conclusion that these patients are either suffering from a different, but equally severe infection or that the PCR tests are not detecting every positive case. Our last hypothesis would be that either immunosuppression (from neoplasia, diabetes or previous steroid use, etc.) may also result in false-negative tests, but the distribution of these factors was similar among the positive and negative test groups.

There is not a clear correlation between an increased BMI and the number of diseases or the probability of death. We consider that this is due to the fact that 85% of our patients have at least one additional disease considered to be a risk factor for poor prognosis with COVID-19 (other than obesity), which makes this a very high-risk group. This may also be related to the lack of health-care education in the population, since regular check-up visits to the general practitioner are not frequent, reflected by the fact that several chronic diseases were diagnosed during the hospitalization. Even when in some cases, the diagnosis needs to be confirmed after the resolution of the sepsis, the previous studies suggest that many of the diseases found during critical illness may persist²⁰. Special efforts must be made to detect relevant comorbidities that may affect the short-term outcome of patients with COVID-19, but also to avoid turning them into long-term victims of their complications²¹. Obesity is a preventable, treatable, but relapsing disease^{22,23} that will warrant further attention and interventions for the COVID-19 survivors and for the general population, since other pandemics may arise in the future²⁴.

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CONFLICTS OF INTEREST

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ETHICAL DISCLOSURES

The protocol was authorized by a National Investigation and Ethics Committee and performed under the guidelines of the Helsinki Declaration of 1975.

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

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