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Original Article

Increased risk of mortality from COVID-19 in people with obesity

Aumento do risco de mortalidade por COVID-19 em pessoas com obesidade

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ABSTRACT

Objective: to analyze the risk of mortality from COVID-19 in people with obesity. **Methods:** observational, retrospective, and analytical study. Data were collected in the State System of Data Analysis. For the comparative analysis of people with and without obesity, n=168,808 was adopted. The analyses were performed using the log-binomial regression model and relative risk calculation. The comparative model was adjusted for sex, age group, heart disease and diabetes. **Results:** in more than 95% of COVID-19 notifications, information regarding the risk factor obesity was recorded as ignored. Obese individuals with COVID-19 had 26% higher risk of death when compared to those without obesity. Obese individuals in the 11 to 60 age groups had the highest mortality risks compared to individuals without obesity. Obese women in the age groups 31 to 50 years and elderly women over 71 years had the lowest mortality risk when compared to obese men. **Conclusion:** obese people, especially adults, have an increased risk of mortality from COVID-19. **Contributions to practice:** to help establish public health strategies to identify the profiles of individuals considered at high risk in the SARS-CoV-2 pandemic.
Descriptors: COVID-19; Obesity; Mortality; Risk Factors.

RESUMO

Objetivo: analisar o risco de mortalidade por COVID-19 em pessoas com obesidade. **Métodos**: estudo observacional, retrospectivo e analítico. Os dados foram coletados no Sistema Estadual de Análise de Dados. Para a análise comparativa de pessoas com e sem obesidade, adotou-se n=168.808. As análises foram realizadas por meio do modelo de regressão log-binomial e cálculo de risco relativo. O modelo comparativo foi ajustado ao sexo, faixa etária, cardiopatia e diabetes. **Resultados**: em mais de 95% das notificações de COVID-19, a informação quanto ao fator de risco obesidade foi registrada como ignorado. Pessoas obesas com COVID-19 apresentaram 26% maior risco de óbito quando comparadas às pessoas sem obesidade. Indivíduos obesos nas faixas etárias entre 11 a 60 anos apresentaram os maiores riscos de mortalidade comparados aos indivíduos sem obesidade. As mulheres obesas nas faixas etárias de 31 a 50 anos e idosas acima de 71 anos apresentaram menor risco de mortalidade quando comparadas aos homens obesos. **Conclusão**: pessoas obesas, principalmente os adultos, possuem risco aumentado de mortalidade por COVID-19. **Contribuições para a prática**: auxiliar o estabelecimento de estratégias de saúde pública que atuem na identificação dos perfis dos indivíduos considerados de alto risco na pandemia ocasionada pelo vírus SARS-CoV-2.
Descritores: COVID-19; Obesidade; Mortalidade; Fatores de Risco.

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Introduction

Obesity has been considered an epidemic and a problem for health systems because of its high prevalence[1]. In Brazil, there has been a gradual increase of obesity in the last two decades, with more than one third of Brazilian males and almost half of females being overweight[2].

Added to this is the fact that obesity offers a greater likelihood of developing other comorbidities such as dyslipidemia, nonalcoholic fatty liver disease, hypertension, diabetes mellitus and depression[3]. In this context, it is highlighted that obesity may also contribute to the worsening of other diseases, including the new coronavirus disease (COVID-19)[4].

The literature points to the association of obesity with an increased risk of death among patients infected by the new coronavirus, with the mortality rate increasing in a manner equivalent to the individual's Body Mass Index (BMI)[5]. Regarding complications from the infection, the results of a systematic review and meta-analysis study corroborate that obese individuals require greater attention and medical surveillance. Thus, obesity is a risk factor for mortality in viral disease since obese individuals have a high risk of developing serious diseases and complications after infection[5-6].

In this context, a study carried out in France showed that the use of invasive mechanical ventilation gradually increased according to the patients' body mass, reaching approximately 90% in individuals with BMI ≥35[7]. Regarding the intensive care unit, patients aged less than 60 years and BMI between 30 and 34 were 2.0 and 1.8 times more likely to be admitted to the unit when compared to individuals in the same age group with BMI <30. Likewise, individuals in the same age group with BMI ≥35 were 2.2 and 3.6 times more likely to be admitted for intensive care than patients under 60 years of age and BMI <30[8].

In Brazil, obesity was the most prevalent group of comorbidities among people hospitalized with COVID-19. The rate of obese hospitalized patients was 11.7%, and of those, 43.4% died[9]. Also, it is noteworthy that in the state of São Paulo, obesity corresponded to approximately 36% of pre-existing diseases among cases of the new coronavirus[10].

Currently, more than five million people have died worldwide due to the infection caused by the virus called Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and obesity has been pointed as a risk factor for the worsening of the disease[5-9]. However, it is necessary to clarify which individuals among the obese population are more susceptible to infection and worsening of the disease. In this context, the aim of this study was to analyze the risk of mortality from COVID-19 in people with obesity.

Methods

This is an observational, retrospective, analytical study. The unit of analysis was the state of São Paulo, which has 46,649,132 million inhabitants according to the Brazilian Institute of Geography and Statistics based on the estimate performed in 2021[11].

The study population comprised 4,003,549 reported cases of COVID-19 in the state of São Paulo, corresponding to the period from February 04, 2020, to July 25, 2021. Cases were included if they had complete data in the database regarding age, sex, death, obesity, heart disease, and diabetes. The sample consisted of 168,808 cases of COVID-19 that met the inclusion criteria.

The variables analyzed in the reported cases of COVID-19 were sex (male and female); age group (0 to 10; 11 to 20; 21 to 30; 31 to 40; 41 to 50; 51 to 60; 61 to 70; 71 to 80; 81 to 90; and older than 90 years); presence of obesity (yes or no); and death. In addition, the variables heart disease and diabetes that could act as confounding factors were included in the analysis.

The data were collected from the State Data Analysis System website, specifically, through the file named "Cases, deaths, and pre-existing diseases". This

is a local system that maintains data related to COVID-19 in the state of São Paulo, available at the state government website[10].

First, the data were described through absolute and percentage frequencies (qualitative variables) such as gender, age group, and obesity, and through measures such as mean, standard deviation, minimum, median, and maximum (quantitative variables) such as age. No specific treatment was adopted for missing (null or empty values). The comparative analyses of individuals in the presence or absence of the obesity risk factor (obesity - yes versus no) were conducted using the log-binomial regression model through the following summary equation: death = obesity + obesity*sex + obesity*age group + sex*age group + obesity*sex*age group + sex + age group + heart disease + diabetes, with consequent calculation of Relative Risk (RR) and its 95% Confidence Intervals (CI). Thus, it was possible to estimate the effect of obesity on mortality adjusted for sex, age group, heart disease and diabetes mellitus and possible confounding variables. For the analyses, we considered a 5% significance level and performed the analyses using the SAS 9.4 software.

The present study used secondary data, of public use and access, available on the official website of the government of the state of São Paulo, thus dispensing with the need for analysis by the Research Ethics Committee, in accordance with Resolution 466/12 of the National Health Council.

Results

The identification of risk factors is an existing field in the COVID-19 notification form, and regarding the risk factor obesity, in 3,823,193 (95.5%) of the notifications, this variable was filled in as ignored, 141,326 (3.5%) of the COVID-19 cases were recorded as being from people without obesity and 39,030 (0.97%) of the cases recorded as being from obese people.

It was estimated that diabetic individuals had, on average, a 9% increase in mortality risk compared to individuals without diabetes. In relation to people with heart disease when compared to people without heart disease, there was no evidence of an association with increased mortality risk in the presence of this comorbidity. When comparing people infected with COVID-19 with and without obesity, it was estimated that obese people had, on average, 26% higher mortality risk when compared to those without obesity ($p<0.01$), regardless of the variables sex, age group, heart disease, and diabetes. Regarding women, it was estimated that those who were considered obese had on average, 35% higher risk of mortality than those without obesity ($p<0.01$). However, in relation to men, the association was null between having or not having obesity with the risk of death ($p=0.120$) (Table 1).

Table 1 – Comparison of the mortality risk for COVID-19 in people with and without obesity in the state of São Paulo (n=168,808). São Carlos, SP, Brazil, 2021

Subgroup	Comparison	RR*	Confidence Interval (95%)	p-value
Heart disease	Heart Disease (Yes vs No)	1.01	0.9998 – 1.02	0.050
Diabetes	Diabetes (Yes vs No)	1.09	1.08 – 1.11	<0.010
Groups	Obesity (Yes vs No)	1.26	1.09 – 1.45	<0.010
Female	Obesity (Yes vs No)	1.35	1.11 – 1.65	<0.010
Male	Obesity (Yes vs No)	1.18	0.96 – 1.44	0.120
With obesity	Female vs Male	1.06	0.80 – 1.40	0.680
Without obesity	Female vs Male	0.92	0.86 – 0.99	0.020
0-10	Obesity (Yes vs No)	1.03	0.27 – 4.00	0.970
11-20	Obesity (Yes vs No)	1.39	0.96 – 2.03	0.080
21-30	Obesity (Yes vs No)	1.39	1.22 – 1.59	<0.010
31-40	Obesity (Yes vs No)	1.50	1.40 – 1.62	<0.010
41-50	Obesity (Yes vs No)	1.54	1.46 – 1.61	<0.010
51-60	Obesity (Yes vs No)	1.38	1.33 – 1.43	<0.010
61-70	Obesity (Yes vs No)	1.24	1.20 – 1.28	<0.010
71-80	Obesity (Yes vs No)	1.14	1.10 – 1.18	<0.010
81-90	Obesity (Yes vs No)	1.06	1.01 – 1.12	0.030
>90	Obesity (Yes vs No)	1.06	0.94 – 1.19	0.340

*RR: Relative Risk, estimated by means of log-binomial regression

The study showed that in the group of individuals with obesity, there was no evidence of a difference in the risk of death between women versus men. However, it was estimated that women without obesity have a lower risk of mortality (7.86%) when compared to men without obesity. Also, people with obesity showed higher mortality risk in almost all age groups when compared to people without obesity, except in the age groups 0 to 20 years and over 90 years. In addition, it was observed that the higher risk of mortality among people with obesity, when compared with people without obesity, gradually decreased after 51 years of age (Table 1).

As for the comparison between people with and without obesity according to gender and age group, according to Table 2, it was estimated that women with obesity aged 11 to 20 years had twice the risk of death than women without obesity (p<0.010). In addition, women with obesity aged 11 to 20 years had 2.03 higher risk of death when compared to men (p=0.030) (Table 2).

In women with obesity aged 0 to 10 years and over 90 years, no evidence was observed in the association of increased mortality risk. However, in the other age groups, as age increases in obese women, a gradual reduction in mortality risk was observed when compared to non-obese women. Also, women with obesity had a higher risk of death in the age groups 21 to 30 years (p<0.01), 41 to 50 years (p<0.01), and 51 to 60 years (p<0.01) when compared to non-obese women (Table 2). In contrast, men with obesity in the age groups 31 to 40 years (p<0.01), 41 to 50 years (p<0.01) and 51 to 60 years (p<0.01) had a higher risk of death when compared to non-obese men. However, in men with obesity in the age groups 0 to 20 years and above 81 years, no evidence was observed in the association with mortality risk (Table 2).

In the comparison by age group and presence of obesity of women versus men, women in the age groups 31 to 40 years, 41 to 50 years, 71 to 80 years, and >90 years had a lower risk of death when compared to men (p=0.040; p=0.040; p=0.020, and p=0.040, respectively). In the analysis by age group and non-obese women versus men, when compared to non-obese men, there was evidence of reduced mortality risk in the age groups 21 to 30 years (p=0.030) and in the age groups >51 years (Table 2).

Table 2 – Comparison of the mortality risk for COVID-19 in people with and without obesity according to sex and age group in the state of São Paulo (n=168,808). São Carlos, SP, Brazil, 2021

Subgroup	Comparison	RR*	Confidence Interval (95%)	p-value
Female				
0 -10	Obesity (Yes vs No)	1.21	0.18 – 8.09	0.840
11-20	Obesity (Yes vs No)	2.00	1.29 – 3.10	<0.010
21-30	Obesity (Yes vs No)	1.60	1.33 – 1.93	<0.010
31-40	Obesity (Yes vs No)	1.41	1.27 – 1.57	<0.010
41-50	Obesity (Yes vs No)	1.50	1.39 – 1.61	<0.010
51-60	Obesity (Yes vs No)	1.46	1.38 – 1.54	<0.010
61-70	Obesity (Yes vs No)	1.31	1.25 – 1.37	<0.010
71-80	Obesity (Yes vs No)	1.19	1.13 – 1.25	<0.010
81-90	Obesity (Yes vs No)	1.09	1.01 – 1.16	0.020
>90	Obesity (Yes vs No)	1.004	0.86 – 1.18	0.960
Male				
0-10	Obesity (Yes vs No)	0.88	0.13 – 6.06	0.890
11-20	Obesity (Yes vs No)	0.97	0.53 – 1.78	0.920
21-30	Obesity (Yes vs No)	1.21	1.00 – 1.45	0.040
31-40	Obesity (Yes vs No)	1.60	1.46 – 1.76	<0.010
41-50	Obesity (Yes vs No)	1.58	1.48 – 1.68	<0.010
51-60	Obesity (Yes vs No)	1.30	1.24 – 1.37	<0.010
61-70	Obesity (Yes vs No)	1.17	1.12 – 1.22	<0.010
71-80	Obesity (Yes vs No)	1.10	1.04 – 1.16	<0.010
81-90	Obesity (Yes vs No)	1.04	0.96 – 1.14	0.360
>90	Obesity (Yes vs No)	1.12	0.94 – 1.32	0.210
With obesity				
0-10	Female vs Male	1.61	0.11 – 23.00	0.720
11-20	Female vs Male	2.03	1.08 – 3.80	0.030
21-30	Female vs Male	1.08	0.90 – 1.31	0.410
31-40	Female vs Male	0.90	0.81 – 1.00	0.040
41-50	Female vs Male	0.92	0.85 – 0.99	0.040
51-60	Female vs Male	0.97	0.91 – 1.03	0.340
61-70	Female vs Male	0.96	0.91 – 1.02	0.160
71-80	Female vs Male	0.92	0.86 – 0.99	0.020
81-90	Female vs Male	0.90	0.81 – 1.00	0.060
>90	Female vs Male	0.79	0.63 – 0.99	0.040
Without obesity	Female vs Male			
0-10	Female vs Male	1.16	0.68 – 2.00	0.580
11-20	Female vs Male	0.98	0.66 – 1.47	0.930
21-30	Female vs Male	0.82	0.68 – 0.98	0.030
31-40	Female vs Male	1.02	0.92 – 1.12	0.720
41-50	Female vs Male	0.97	0.91 – 1.03	0.350
51-60	Female vs Male	0.87	0.83 – 0.90	<0.010
61-70	Female vs Male	0.86	0.83 – 0.88	<0.010
71-80	Female vs Male	0.85	0.83 – 0.87	<0.010
81-90	Female vs Male	0.86	0.84 – 0.89	<0.010
>90	Female vs Male	0.88	0.84 – 0.92	<0.010

*RR: Relative Risk, estimated by means of log-binomial regression

Discussion

This study evidenced that obese individuals showed increased risk of mortality from COVID-19 when compared to individuals without obesity. These results corroborate the literature, showing obesity associated with increased mortality risk[4-6].

Obese people infected with the new coronavirus were more likely to progress to the severe form of the disease compared to people of normal weight, since the association remained significant after adjusting for comorbidities and other risk factors[12]. Moreover, for each 1 kg/m^2 increase in BMI, the risk of developing the severe form of the disease and death increased by 9 and 6%, respectively[13].

The relationship between obesity and the disease caused by SARS-CoV-2 is not fully understood, but its explanation may be related to the fact that obese people have higher concentrations of the hormone leptin and lower concentrations of adiponectin, resulting in the inefficient performance of defense lines in the immune response. In addition, these individuals have higher concentrations of pro-inflammatory cytokines, and, under viral infection, the chronic inflammation linked to obesity provides a reduction in macrophage activation and weakens the production of pro-inflammatory cytokines after macrophage stimulation. This dysregulated pro-inflammatory response would contribute to the severe lung lesions in the disease infection[14-15].

In addition, obesity leads to fat accumulation in the ribs, diaphragm, and abdomen, resulting in attenuation of lung functional capacity, respiratory system compliance, and lung expiratory reserve volume. Taken together, the weakening of the respiratory system in obese individuals can be severely compromised by any respiratory insults, which means that these patients will have difficulty recovering if they have developed any serious disease that can negatively affect respiratory function[16].

These physiological changes resulting from obesity may explain the findings found in the United States, where overweight or obese individuals, compared to people of normal weight, presented more symptoms, especially respiratory symptoms that included cough and shortness of breath[17].

It is noteworthy that the main risk factors described in children and adolescents that relate obesity to COVID-19 are the same as those observed in adults, i.e., obesity alters the immune system resulting in a pro-inflammatory state, contributing to the emergence or exacerbation of several diseases[4,16,18].

Regarding self-reported symptom frequency, duration and severity levels by overweight and obese adolescents were like those of adults. Adolescents had more symptoms with higher self-reported severity that lasted longer than children under 12 years of age[17]. This finding may indicate an absence of symptoms or mild symptoms in younger children that may not be associated with SARS-CoV-2 infection, which may make diagnosis difficult and result in underreporting in this population group.

Furthermore, the literature points out that the angiotensin-converting enzyme 2 (ACE 2), which has a high concentration in the heart and lung, is used by the spike protein of the SARS-CoV-2 virus as a receptor to enter the host cell. However, in the adipose tissue, its expression is higher than in the lung tissue, so obese individuals would have a higher amount of the enzyme, leading to the hypothesis that excess adipose tissue could contribute to the development of severe cases of the disease[16,18].

Besides the physiological mechanisms related to obesity and the new coronavirus, the poor prognosis of obese patients may be related to the individual's gender. In this context, the literature points out that the virus infects all age groups and sexes; however, a prevalence has been observed in males, and especially in those with chronic diseases among the most severely affected[19]. It is noteworthy that sex differences related to SARS-CoV-2 infection have already been observed in a previous epidemic[20].

Stratification by sex revealed worse outcomes in males compared to females with higher risks of

death and intubation in males with obesity. Further, stratified analysis showed that younger patients with obesity between 45 and 64 years of age have a relative risk of three for intubation compared to younger patients with normal BMI, while patients aged 65 years and older have a comparatively lower relative risk of 2.1[21]. In this scenario, a higher mortality risk has been observed in men compared to women, and the explanations for sex differences in coronavirus infection are not yet fully understood.

Thus, one mechanism that may explain the greater susceptibility of men to develop the severe form of the disease may be related to the X chromosome and sex hormones. It is noteworthy that many genes are located on the X chromosome, including important genes related to the immune system. In women, genotype XX, a process called X-chromosome inactivation prevents the overexpression of X-linked genes; however, some genes can escape this process and double their expression. Consequently, the overexpression of immune system genes could present a stronger immune response to viral infections compared to men[22-23].

Regarding sex hormones and their influence before viral infections, it is noteworthy that these have changes in their levels according to age, besides the physiological state of the individual[23]. It is worth noting that in both sexes, the onset of puberty is marked by an increase in hormone production. On the other hand, a significant reduction in estradiol and progesterone serum levels and an increase in follicle stimulating hormone and luteinizing hormone levels are observed at menopause. In men, associated with aging, a more gradual decrease in testosterone levels is observed compared to the drop in female hormone levels[24].

In an analysis regarding the protection of female hormones it was observed that menopausal women and men of the same age showed no apparent differences in terms of clinical severity in COVID-19 disease. However, compared to men of the same age, fewer non-menopausal women suffered from the disease in its severe form[25].

However, besides the possible hormonal influence observed, among the various reasons for the differential response in individuals to coronavirus, age is also presented as an important risk factor for the progression of the severe form of the infection, and the number of individuals with obesity gradually decreases as age increases due to survivorship bias, as obesity is associated with reduced life expectancy[26].

It is noteworthy that obesity in general was associated with a 4.2-year reduction in life expectancy in men and 3.5 years in women; class 3 obesity was associated with a 9.1-year reduction in life expectancy in men and 7.7 years in women. Furthermore, the associations between BMI and mortality were stronger at younger ages than at older ages, and higher degrees of obesity were strongly associated with overall and cardiovascular mortality in men than in women[27].

However, aging is known to contribute to functional decline in both the innate and adaptive immune systems. Recently, it has been evidenced that coronaviruses target ACE receptors 2 and the enzyme dipeptidyl peptidase-4, also known as CD26, found in diversity in cells, and both receptors are highly expressed in senescent cells, which would cause an increased lethality rate in people infected with the SARS-CoV-2 virus. However, besides the decline of the immune system in the aging process, when associated with chronic inflammation resulting from obesity, an inefficient response to viral infections is expected, which may result in increased mortality among obese elderly[28].

Thus, an alternative to reduce mortality caused by coronavirus, especially among those who are more susceptible to infection, is vaccination. However, there is concern about the reduced efficacy of vaccination in obese people, describing that obesity is associated with reduced memory immune responses, leading to decreased long-term protection against reinfection[29].

It is noteworthy that the alpha, beta, gamma, delta, and omicron variants are currently circulating around the world and in Brazil, making wide adherence to vaccination essential, especially in underdevelo-

ped countries. Therefore, the relaxation of protective measures, especially in groups considered at risk, will only be possible after effective control of the pandemic[30].

Study limitations

This study has limitations such as the large percentage of ignored in relation to the risk factor obesity recorded in the notification forms of the disease caused by the new coronavirus, this absence of data may influence the interpretation of the results due to the limitation of the sample obtained. Finally, it was not possible to analyze variables regarding the degree of obesity, presence of other comorbidities, race/ethnicity, and socioeconomic and environmental factors that could relate to a worse prognosis of COVID-19.

Contributions to practice

This study minimizes the gap in the literature on the topic by describing which individuals among the obese population are at increased risk of mortality in coronavirus infection. Furthermore, it may contribute to the establishment of public health strategies that identify and track changes in the profiles of people considered at high risk in pandemic COVID-19.

Conclusion

This was a comprehensive analysis on the mortality of COVID-19 in people with obesity, evidencing that people with some degree of obesity have an increased risk of mortality when compared to people without obesity. Furthermore, the study showed that in males, especially, in the age group ranging from 31 to 60 years, the presence of obesity may contribute to increased mortality in SARS-CoV-2 infection.

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Authors' contribution

Conception, planning, analysis, interpretation, writing of the work, relevant critical review of the intellectual content, final approval of the version to be published and responsibility for all aspects of the manuscript: Ribeiro AC, Uehara SCSA.

Interpretation and writing of the work, final approval of the version to be published, and responsibility for all aspects of the manuscript: Poli P.

References

1. Yoon J. Prevalence of obesity and incidence of obesity-related comorbidities in Koreans based on national health insurance service health checkup data 2006-2015. J Obes Metab Syndr 2018;27:46-52. doi: https://dx.doi.org/10.7570/jomes.2018.27.3.195
2. Instituto Brasileiro de Geografia e Estatística (IBGE). Pesquisa Nacional de Saúde 2019: atenção primária à saúde e informações antropométricas [Internet]. 2020 [cited Aug 29, 2022]. Available from: https://biblioteca.ibge.gov.br/visualizacao/livros/liv101758.pdf
3. Bliss ES, Whiteside E. The gut-brain axis, the human gut microbiota and their integration in the development of obesity. Front Physiol. 2018;9:900. doi: https://doi.org/10.3389/fphys.2018.00900
4. Nogueira-de-Almeida CA, Del Ciampo LA, Ferraz IS, Del Ciampo IRL, Contini AA, Ued FDV. COVID-19 and obesity in childhood and adolescence: a clinical review. J Pediatr (Rio J). 2020;96(5):546-8. doi: https://doi.org/10.1016/j.jped.2020.07.001
5. Poly TN, Islam MM, Yang HC, Lin MC, Jian WS, Hsu MH, et al. Obesity and mortality among patients diagnosed with COVID-19: a systematic review and meta-analysis. Front Med (Lausanne). 2021;8:620044. doi: https://dx.doi.org/10.3389/fmed.2021.62004

6. Yang J, Hu J, Zhu C. Obesity aggravates COVID-19: a systematic review and meta-analysis. J Med Virol. 2021;93(1):257-61. doi: 10.1002/jmv.26237

7. Simonnet A, Chetboun M, Poissy J, Raverdy V, Noulette J, Duhamel A, et al. High prevalence of obesity in Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) requiring invasive mechanical ventilation. Obesity (Silver Spring). 2020;28(7):1195-9. doi: http://doi.org/10.1002/oby.22831

8. Lighter J, Phillips M, Hochman S, Sterling S, Johnson D, Francois F, et al. Obesity in patients younger than 60 years is a risk factor for COVID-19 hospital admission. Clin Infect Dis. 2020;71(15):896-7. doi: https://doi.org/10.1093/cid/ciaa415

9. Souza FSH, Hojo-Souza NS, Batista BDO, Silva CM, Guidoni DL. On the analysis of mortality risk factors for hospitalized COVID-19 patients: a data-driven study using the major Brazilian database. PLoS One. 2021;16(3):e0248580. doi: https://doi.org/10.1371/journal.pone.0248580

10. Fundação Sistema Estadual de Análise de Dados - SEADE. Boletim completo [Internet]. 2022 [cited Apr 11, 2022]. Available from: https://www.seade.gov.br/coronavirus/#

11. Instituto Brasileiro de Geografia e Estatística (IBGE). População [Internet]. 2021 [cited Apr 2, 2022]. Available from: https://cidades.ibge.gov.br/brasil/sp/panorama

12. Cai Q, Chen F, Wang T, Luo F, Liu X, Wu Q, et al. Obesity and COVID-19 severity in a designated hospital in Shenzhen, China. Diabetes Care. 2020;43(7):1392-8. doi: https://doi.org/10.2337/dc20-0576

13. Du Y, Lv Y, Zha W, Zhou N, Hong X. Association of body mass index (BMI) with critical COVID-19 and in-hospital mortality: a dose-response meta-analysis. Metabolism. 2021;117:154373. doi: https://doi.org/10.1016/j.metabol.2020.154373

14. Yu W, Rohli KE, Yang S, Jia P. Impact of obesity on COVID-19 patients. J Diabetes Complications. 2021;35(3):107817. doi: http://dx.doi.org/10.1016/j.jdiacomp.2020.107817

15. Kim J, Nam JH. Insight into the relationship between obesity-induced low-level chronic inflammation and COVID-19 infection. Int J Obes. 2020;44:1541-2. doi: https://dx.doi.org/10.1038/s41366-020-0602-y

16. Albashir AAD. The potential impacts of obesity on COVID-19. Clin Med (Lond). 2020;20(4):e109-e113. doi: https://dx.doi.org/10.7861/clinmed.2020-0239

17. Cheng WA, Turner L, Marentes Ruiz CJ, Tanaka ML, Congrave-Wilson Z, Lee Y, et al. Clinical manifestations of COVID-19 differ by age and obesity status. Influenza Other Respir Viruses. 2022;16(2):255-64. doi: https://doi.org/10.1111/irv.12918

18. Emilsson V, Gudmundsson EF, Aspelund T, Jonsson BG, Gudjonsson A, Launer LJ, et al. Serum levels of ACE2 are higher in patients with obesity and diabetes. Obes Sci Pract. 2020;7(2):239-43. doi: https://doi.org/10.1002/osp4.472

19. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. China medical treatment expert group for covid-19. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020;382(18):1708-20. doi: http://doi.org/10.1056/NEJMoa2002032

20. Abdolmaleki G, Taheri MA, Paridehpour S, Mohammadi NM, Tabatabaei YA, Mousavi T, et al. A comparison between SARS-CoV-1 and SARS-CoV2: an update on current COVID-19 vaccines. Daru J Pharm Sci. 2022;1-28. doi: https://doi.org/10.1007/s40199-022-00446-8

21. Nakeshbandi M, Maini R, Daniel P, Rosengarten S, Parmar P, Wilson C, et al. The impact of obesity on COVID-19 complications: a retrospective cohort study. Int J Obes (Lond). 2020;44(9):1832-7. doi: https://doi.org/10.1038/s41366-020-0648-x

22. Brandi ML. Are sex hormones promising candidates to explain sex disparities in the COVID-19 pandemic? Rev Endocr Metab Disord. 2022;23(2):171-83. https://dx.doi.org/10.1007/s11154-021-09692-8

23. Schurz H, Salie M, Tromp G, Hoal EG, Kinnear CJ, Möller M. The X chromosome and sex-specific effects in infectious disease susceptibility. Hum Genomics. 2019;13(1):2. https://doi.org/10.1186/s40246-018-0185-z

24. Shepherd R, Cheung AS, Pang K, Saffery R, Novakovic B. Sexual dimorphism in innate immunity: the role of sex hormones and epigenetics. Front Immunol. 2021;11:604000. doi: https://doi.org/10.3389/fimmu.2020.604000

25. Ding T, Zhang J, Wang T, Cui P, Chen Z, Jiang J, et al. Potential influence of menstrual status and

sex hormones on female severe acute respiratory syndrome coronavirus 2 infection: a cross-sectional multicenter study in Wuhan, China. Clin Infect Dis. 2021;72(9):e240-e248. doi: https://doi.org/10.1093/cid/ciaa1022

26. Halpern B, Louzada MLDC, Aschner P, Gerchman F, Brajkovich I, Faria-Neto JR, et al. Obesity and COVID-19 in Latin America: a tragedy of two pandemics-official document of the Latin American Federation of Obesity Societies. Obes Rev. 2021;22(3):e13165. doi: https://doi.org/10.1111/obr.13165

27. Bhaskaran K, Santos-Silva I, Leon DA, Douglas IJ, Smeeth L. Association of the BMI with overall and cause-specific mortality: a population-based cohort study of 3·6 million adults in the UK. Lancet. 2018;6(12):944-53. doi: https://dx.doi.org/10.1016/S2213-8587(18)30288-2

28. Al-Bari MAA, Hossain S, Zahan MK. Exploration of sex-specific and age-dependent COVID-19 fatality rate in Bangladesh population. World J Radiol. 2021;13(1):1-18. doi: https://doi.org/10.4329/wjr.v13.i1.1

29. Westheim AJF, Bitorina AV, Theys J, Shiri-Sverdlov R. COVID-19 infection, progression, and vaccination: focus on obesity and related metabolic disturbances. Obes Rev. 2021;22(10):e13313. doi: https://doi.org/10.1111/obr.13313

30. Siqueira PC, Cola JP, Comerio T, Sales CMM, Maciel EL. Herd immunity threshold for SARS-CoV-2 and vaccination effectiveness in Brazil. J Bras Pneumol. 2022;48(2):e20210401. doi: https://dx.doi.org/10.36416/1806-3756/e20210401