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Mortality from COVID-19 in people with heart disease in São Paulo State

Mortalidade por COVID-19 em pessoas cardiopatas no estado de São Paulo

Mortalidad por COVID-19 en cardiópatas en el estado de São Paulo

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ABSTRACT

Objective: to examine mortality from the disease caused by type-2 Coronavirus (COVID-19) in people with heart disease in São Paulo State. **Methods:** in this, retrospective, analytical, observational study, data were collected from February 4, 2020, to July 25, 2021. The model comparing people with and without heart disease was adjusted for the possible confounding variables sex, age group, obesity, and diabetes. Comparisons were analyzed using log-binomial regression models and relative risk calculation. **Results:** risk of death was higher among people between 21 and 50 years old infected by COVID-19 and with heart disease than among people without heart disease. Also, risk of death was lower among women with heart disease over 51 years old than among men with heart disease in the same age group. **Conclusion:** people, especially men, with heart disease and infected by COVID-19 are at increased risk of death.

Descriptors: COVID-19; Cardiovascular Diseases; Risk Factors; Mortality.

RESUMO

Objetivo: analisar a mortalidade pela doença causada pelo coronavírus do tipo 2 (COVID-19) em pessoas com cardiopatia no estado de São Paulo. **Métodos**: estudo observacional, retrospectivo e analítico. Os dados foram coletados no período de 4 de fevereiro de 2020 a 25 de julho de 2021. O modelo comparando pessoas com e sem cardiopatia foi ajustado por sexo, faixa etária, obesidade e diabetes, possíveis variáveis de confusão. As comparações foram analisadas por meio do modelo de regressão log-binomial e cálculo de risco relativo. **Resultados**: pessoas do estado de São Paulo com cardiopatia infectadas pela COVID-19 entre 21 e 50 anos apresentaram risco maior de óbito quando comparadas as pessoas sem cardiopatia. Ainda, mulheres cardiopatas acima de 51 anos apresentaram risco menor de óbito comparadas aos homens cardiopatas na mesma faixa etária. **Conclusão**: pessoas com cardiopatia infectadas pelo COVID-19, principalmente homens, possuem um risco aumentado de morte no estado de São Paulo.

Descritores: COVID-19; Doenças Cardiovasculares; Fatores de Risco; Mortalidade.

RESUMEN

Objetivo: analizar la mortalidad por la enfermedad causada por el coronavírus del tipo 2 (COVID-19) en personas cardiópatas en el estado de São Paulo. **Métodos:** estudio observacional, retrospectivo y analítico. Los datos se recopilaron del 4 de febrero de 2020 al 25 de julio de 2021. El modelo que compara personas con y sin cardiopatía se ajustó por sexo, grupo de edad, obesidad y diabetes, posibles variables de confusión. Las comparaciones se analizaron mediante el modelo de regresión log-binomial y el cálculo del riesgo relativo. **Resultados:** las personas del estado de São Paulo, con cardiopatías, infectadas por COVID-19 entre 21 y 50 años tenían mayor riesgo de muerte en comparación con las personas sin cardiopatías. Además, las mujeres con cardiopatías mayores de 51 años tenían un menor riesgo de muerte en comparación con los hombres con cardiopatías del mismo grupo de edad. **Conclusión:** las personas con cardiopatías infectadas por COVID-19, especialmente los hombres, tienen mayor riesgo de muerte, en el estado de São Paulo.

Descriptores: COVID-19; Enfermedades Cardiovasculares; Factores de Riesgo; Mortalidad.

INTRODUCTION

On March 11th, 2020, the World Health Organization (WHO) declared a pandemic situation for the disease caused by the type 2 coronavirus (COVID-19). The disease comprises a severe acute illness that affects the respiratory system, constituting, to the present day, a public health emergency of international importance[1].

It is known that the infection caused by the *Severe Acute Respiratory Syndrome – Coronavirus – 2* (SARS-CoV-2) develops symptoms of mild to severe intensity. However, it should be noted that the COVID-19 symptoms have changed as new variants of the virus emerged since the beginning of the pandemic[2].

At the beginning of the pandemic period, the most common symptoms observed included fever, dry cough, difficulty breathing, tiredness and loss of taste or smell. Currently, in addition to the already known symptoms, runny nose, vomiting, diarrhea, extreme tiredness, muscle aches, headache and sore throat have been reported related to the new variants[2].

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However, although the COVID-19 complications mainly involve the respiratory system, SARS-CoV-2 can reach and damage other organs such as the liver, kidneys, heart and venous system[3]. It is noted that the complications associated with the cardiovascular system contribute to the mortality rate due to COVID-19. In addition to that, among the factors that contribute to complications, when an individual develops the aforementioned disease, we find the underlying comorbidities, especially cardiovascular ones, including systemic arterial hypertension in addition to diabetes[3,4].

In this context, the literature points out that individuals with pre-existing Cardiovascular Diseases (CVDs) are at an increased risk of death when they contract COVID-19[4,5]. SARS-CoV-2 can interact with the cardiovascular system at multiple levels, increasing morbidity in patients with underlying cardiovascular conditions and causing myocardial injury and dysfunction[4]. In addition, the increase in mortality among individuals with cardiovascular diseases can be associated with younger age groups and those with compromised immune systems[4,5].

Faced with a possible association between CVDs and unfavorable COVID-19 outcomes, it is essential to conduct studies that clarify which individuals belonging to the population with CVDs are at a higher risk of mortality due to the COVID-19 disease.

In this sense, this study aimed at analyzing the risk of mortality due to COVID-19 among people with heart disease in the state of São Paulo.

METHOD

This is an observational, retrospective and analytical study. The unit of analysis was the state of São Paulo, which has 46,649,132 inhabitants according to the estimate carried out in 2021 by the Brazilian Institute of Geography and Statistics (*Instituto Brasileiro de Geografia e Estatística*, IBGE)[6].

The study population consisted of 4,003,549 COVID-19 cases reported in the state of São Paulo, from February 4th, 2020, to July 25th, 2021. All the COVID-19 cases notified in the state of São Paulo that presented complete information regarding age, gender, death, heart disease, obesity and diabetes were included. Thus, only the notified COVID-19 cases that were not complete in terms of data recording were excluded from the analysis. Thus, the sample consisted of 168,808 COVID-19 cases.

The data were collected on the "*Boletim completo*" ("Full Bulletin") website, specifically from the file called "*Casos, óbitos e doenças preexistentes*" ("Cases, deaths and pre-existing diseases"), made available by the State Data Analysis System (*Sistema Estadual de Análise de Dados*, SEADE), belonging to the government of the state of São Paulo.

SEADE is a local system that maintains an electronic data panel updated daily where cases and deaths related to the coronavirus in Brazil and in the world are described, with a focus on the state of São Paulo. The information is publicly accessible and Comma-Separated Values (CSV) data are available, which can be downloaded without restrictions from https://www.seade.gov.br/coronavirus/[7].

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

Initially, the data were described using absolute and percentage frequencies (qualitative variables) and via measures such as mean, standard deviation, minimum, median and maximum (quantitative variables). In the comparative analysis of the individuals with or without the heart disease risk factor (heart disease - yes versus no), they were analyzed using the log-binomial regression model, with consequent calculation of Relative Risks (RR) and their 95% Confidence Intervals ($CI_{95\%}$). In addition to that, the comparative model of individuals with and without heart disease was adjusted for gender, age group, obesity and diabetes *mellitus*, possible confounding variables. For the analyses, a 5% significance level was considered and they were performed using the SAS® 9.4 software.

The current study resorted to secondary data of public use and access, available on the official website of the government of the state of São Paulo, being exempt from appreciation by any Ethics Committee in Research involving human beings, in accordance with Resolution No. 466⁄12 of the National Health Council.

RESULTS

The identification of risk factors is a field included in the notification form of COVID-19 cases; however, when analyzing the database, most of the information regarding comorbidities was found as "Unknown". In relation to heart disease, it was observed that, in 89.78% of the cases (n=3,594,232), the information was reported as "Unknown". In turn, 8.35% of the cases had some heart disease (n=334,103) and 1.88% had no heart diseases (n=75,214).

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Table 1 shows the comparison of the mortality risk in the sample under study without gender or age group distinctions.

TABLE 1: Comparison of the risk of mortality due to COVID-19 among individuals with and without heart disease in the state of São Paulo. São Carlos, SP, 2021.

Subgroup	RR	Confidence Interval (95%)	p-value
All	1.09	0.99-1.21	0.08
Female	1.10	0.94-1.28	0.22
Male	1.09	0.95-1.24	0.22
0-10	1.21	0.53-2.75	0.65
11-20	1.36	0.79-2.35	0.27
21-30	1.24	1.06-1.45	<0.01
31-40	1.14	1.06-1.23	<0.01
41-50	1.05	1.00-1.10	0.04
51-60	1.02	0.98-1.05	0.33
61-70	1.01	0.99-1.04	0.29
71-80	1.01	0.98-1.04	0.45
81-90	0.97	0.95-1.00	0.05
>90	0.99	0.94-1.04	0.65

In the comparative analysis of the mortality risk of people infected by COVID-19 with heart disease versus those without heart disease, both in the “All” subgroup (p=0.08), which covers all individuals without gender or age group distinctions, and in the “Female” (p=0.22) and “Male” (p=0.22) subgroups there was no statistically significant evidence regarding higher risk of death in people with heart disease.

However, when comparing people with heart disease versus people without heart disease by age group, there was a statistically significant difference regarding the risk of death in the age groups from 21 to 30 years old (p<0.01), from 31 to 40 years old (p <0.01) and from 41 to 50 years old (p=0.04), showing that people with heart disease belonging to these age groups were at a higher risk of death when compared to those without heart disease.

Table 2 presents the analysis results, considering gender and age group.

Regarding the comparison of people with heart disease versus those without heart disease, in the analysis of the female gender according to age group, women with heart disease in the age groups from 11 to 20 years old (p<0.01), from 21 to 30 years old (p =0.02), from 31 to 40 years old (p<0.01) and from 41 to 50 years old (p<0.01), were at a higher risk of death when compared to those without heart disease. In addition to that, in the age group from 11 to 20 years old, women with heart disease presented 2.10 times the risk of death when compared to those without heart disease. In the male gender, in this same comparison, only in the age group from 81 to 90 years old (p<0.01) did men with heart disease have a higher risk of death due COVID-19.

When performing the analysis of people with heart disease between age groups, comparing females versus males, it was evidenced that women with heart disease in the age groups over 51 years old were at a lower risk of death than men of the same age (p<0.01). A similar result was observed among people without heart disease; however, the lower risk of death in females when compared to males has already been observed after 31 years of age.

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TABLE 2: Comparison of the risk of mortality due to COVID-19 among individuals with and without heart disease in the state of São Paulo, according to gender and age group. São Carlos, SP, 2021.

Subgroup		RR	Confidence Interval (95%)		p-value
Female	0-10	0.64	0.16	2.61	0.54
	11-20	2.10	1.23	3.59	<0.01
	21-30	1.32	1.05	1.65	0.02
	31-40	1.23	1.10	1.38	<0.01
	41-50	1.11	1.03	1.19	<0.01
	51-60	1.03	0.98	1.08	0.32
	61-70	1.02	0.98	1.06	0.37
	71-80	1.02	0.98	1.06	0.34
	81-90	0.99	0.95	1.03	0.75
	>90	1.02	0.95	1.09	0.61
Male	0-10	2.27	0.97	5.34	0.06
	11-20	0.88	0.34	2.28	0.79
	21-30	1.17	0.94	1.45	0.15
	31-40	1.05	0.95	1.16	0.32
	41-50	1.00	0.94	1.06	1.00
	51-60	1.01	0.97	1.05	0.74
	61-70	1.01	0.98	1.04	0.55
	71-80	1.00	0.97	1.03	0.98
	81-90	0.95	0.92	0.99	<0.01
	>90	0.96	0.90	1.03	0.26
Female vs Male					
0-10	With	0.40	0.09	1.87	0.24
11-20	heart	2.63	0.93	7.39	0.07
21-30	diseases	1.03	0.78	1.35	0.84
31-40		1.07	0.95	1.21	0.28
41-50		1.01	0.94	1.08	0.75
51-60		0.90	0.87	0.94	<0.01
61-70		0.88	0.85	0.90	<0.01
71-80		0.86	0.84	0.88	<0.01
81-90		0.87	0.85	0.90	<0.01
>90		0.88	0.84	0.94	<0.01
Female vs Male					
0-10	Without	1.42	0.80	2.53	0.23
11-20	heart	1.10	0.77	1.58	0.61
21-30	diseases	0.91	0.79	1.06	0.23
31-40		0.91	0.83	1.00	0.04
41-50		0.91	0.86	0.98	<0.01
51-60		0.89	0.85	0.93	<0.01
61-70		0.87	0.84	0.91	<0.01
71-80		0.84	0.81	0.88	<0.01
81-90		0.84	0.80	0.88	<0.01
>90		0.84	0.77	0.90	<0.01

DISCUSSION

In the current study, it was identified that, in 89.78% of the COVID-19 cases, the information regarding the risk factor on the presence or absence of heart disease was reported as “Unknown”. Thus, the incompleteness of the COVID-19 notification forms imposes limitations on the epidemiological and social analyses, interfering with the identification of population groups most susceptible to COVID-19 and, consequently, exerting direct impacts on the planning of actions and public health resources directed to fight against the pandemic[8].

It is known that the COVID-19 pandemic affected millions of people and represents a threat to human health to the present day, and the literature has been pointing out that mortality due to COVID-19 is associated with the presence of comorbidities, including CVDs[9,10]. A study conducted in China with 44,672 COVID-19 cases showed that the overall lethality rate was higher among those with pre-existing comorbidities, with 10.5% for CVDs[11].

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The death cases in children reported to the WHO in the period from December 30th, 2019, to October 25th, 2021, represent less than 1% of the global deaths. Since the beginning of the pandemic, it has been observed that children are generally less likely to contract COVID-19 when compared to adults and that, when infected, they usually have mild conditions, ranging from flu-like symptoms to no symptoms. However, although the clinical presentation of COVID-19 is milder when compared to adults and aged people, underlying medical conditions may contribute to the risk of serious disease when compared to children with no reported underlying medical conditions[12].

The results of this study showed that children with heart disease were not at a higher risk of death due to COVID-19 when compared to those without heart disease. However, a meta-analysis including 275,661 children without comorbidities and 9,353 children with comorbidities, showed that severe COVID-19 was present in 5.1% of the children with comorbidities and in 0.2% of those without comorbidities, as well as that children with underlying disease also had a 2.81 times higher risk of death associated with COVID-19[13].

Children with congenital heart disease can develop serious cardiovascular complications related to COVID-19, with greater chances of admission to Intensive Care Units (ICUs) and artificial respiratory support. In addition to that, children with complex cardiac comorbidities and COVID-19 can develop severe and critical conditions, such as depression of myocardial contractility and pulmonary hypertension[14].

As for the COVID-19 infection, a study carried out in India involving 94 children and adolescents under eighteen years of age showed that, in addition to children with heart disease, those belonging to lower socioeconomic classes and with severe diseases were at a higher risk of death related to the COVID-19 disease[15]. The influence of socioeconomic factors on COVID-19 evidences that an increase in adherence to the quarantine restrictions was associated with people with a high schooling levels[16].

However, in addition to underlying comorbidities such as CVDs, which are risk factors for unfavorable outcomes in COVID-19, the emergence of new variants considered to be of global concern stands out. Among them, the *gamma* variant (P.1) stands out, which has become a concern in Brazil due to the increase in the number of COVID-19 cases at the beginning of 2021; and more recently, in January 2022, the *omicron* variant, which, although presenting itself as a mild disease in most cases, results in a lower detection rate and therefore contributes to greater transmission[14,15,17,18].

Omicron spread across the world in mid-January 2022, causing an increase in the number of COVID-19 cases, interrupting a downward trend in the number of cases and deaths caused by SARS-CoV-2. In the state of São Paulo, in the 3rd epidemiological week of 2022 (January 16th to January 22nd) *omicron* already accounted for 99.7% of the positive samples sequenced in the state of São Paulo[18].

In this scenario, there was a 61.3% increase in the number of patients under the age of 18 admitted to ICUs, in the comparison between January 17th, 2022, and November 15th, 2021[19]. A similar increase in cases was observed in the state of Santa Catarina, where the occupancy rate of Pediatric ICU beds for the treatment of COVID-19 grew 433% in the first half of February 2022[20].

According to the National Vaccination Operational Plan (*Plano de Nacional de Operacionalização a Vacinação*, PNOV) against COVID-19, as of July 2022, vaccination was indicated for the entire Brazilian population from 3 years of age; however, there is no obligation regarding immunization against COVID-19 in children aged 5 to 11[12].

In addition to that, in the state of São Paulo, until December 15th, 2022, only 45.14% of the children eligible for vaccination had the complete vaccination schedule for COVID-19[21]. Therefore, low adherence to childhood vaccination may contribute both to the increase in mortality among this population and to the dissemination of new SARS-CoV-2 variants.

In relation to the COVID-19 infection observed in adults with CVDs, a review study showed that some patients with congenital heart disease are at a greater risk when compared to the presence of other types of heart diseases. These conditions can be considered at high risk for complications related to the COVID-19 infection based on decreased functional reserve[14].

In this study, women aged from 11 to 20 years old with heart disease were found to have twice the risk of death when compared to those without heart disease, and people aged between 21 and 50 years old with heart disease were at a higher risk of death when compared to those without heart disease. In addition to that, women with heart disease in the age groups above 51 years old had a lower risk of death than males.

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A similar result was observed in people without heart disease; however, the lower risk of death in women when compared to men was already lower after 31 years of age. These findings suggest that age, as well as being female, may have protective effects; however, the presence of CVDs can minimize this protection against the SARS-CoV-2 infection.

A meta-analysis including more than three million COVID-19 cases showed that, although there is no difference in the proportion of men and women with COVID-19, male patients were almost three times more likely to require ICU admission and to present higher chances of death when compared to women[22,23].

With few exceptions, the gender bias seen in COVID-19 is a worldwide phenomenon and some factors may be attributable to worsening of the COVID-19 infection in males. In this sense, in Italy it was verified that women were more likely to adhere to the preventive measures against SARS-CoV-2 when compared to men[16].

However, in addition to socioeconomic and environmental factors that can contribute to COVID-19 worsening, men and women respond differently to viral infections. While gender-based immunological differences are not new, gender as a biological variable is often overlooked in clinical research, and COVID-19 is no exception.

It is noted that studies referring to the SARS-CoV infection, which were conducted between 2002 and 2004, had already reported that men presented a higher mortality rate when compared to women: 21.9% versus 13.2%, respectively[24].

In addition to that, a previous COVID-19 study related to vaccines described that among children, young adults and aged people, men and women differ in vaccine-induced immune responses, adverse events and protection. Women generally develop higher antibody responses and report more adverse effects from vaccination than men[25]. This suggests a need for gender-differentiated dosage regimens, as the evidence indicates that women have better immune responses when compared to men; these findings may influence the development of strategies both for COVID-19 treatment and vaccination.

In addition to sexual dimorphism in the immune system, it is necessary to consider age-related changes in the immune system that are also different between the genders. In the scenario where there is a marked association between morbidity and mortality and advanced age among people with COVID-19, a study conducted in Turkey showed that, as age increased, the number of intubated patients and ICU deaths also increased[26].

Although the literature points out that COVID-19 severity is associated with comorbidities, including CVDs, it is still unclear whether these diseases specifically contribute to development of the SARS-CoV-2 pathogenesis or if they are mainly biological age indicators.

Aging can result in changes in the immune system, such as the gradual decline in immune function, which may decrease the ability to eliminate SARS-CoV-2. The ability to control viral load is one of the best predictors of whether a patient will have mild or severe COVID-19 symptoms[27].

However, elucidation of the SARS pathogenesis is complicated because COVID-19 and CVDs share another common feature, Angiotensin Converting Enzyme 2 (ACE2), which is involved in the pathogenesis of both[27]. Among the hypotheses that could explain an association between pre-existing CVDs and death due to COVID-19 are differences in ACE2 expression or function. Such interactions could simultaneously predispose to the development of CVDs and, thereby, considerably increase the likelihood or severity of SARS-CoV-2 infection[28].

Thus, once again, the role of sexual dimorphism in the incidence of COVID-19 is highlighted, as many genes that play important roles in the immune responses are present on the X chromosome. In the COVID-19 infection, the ACE2 gene, the receptor mainly responsible for the cellular entry of SARS-CoV-2, is present on the X chromosome, where up to 30% of the genes suffer inactivation escape and, therefore, increased expression in women could contribute to the female protective effect observed in the COVID-19 pandemic[29].

In addition to that, gender differences in the manifestation of infectious diseases are attributed to the influence of sex hormones, such as estrogen, which promote the expression of ACE2. In men, low estrogen levels result in the absence of higher ACE2 levels, supporting the ACE pathway in the Renin Angiotensin System (RAS) axis that favors disease severity in men even if having the same viral load as women[29].

Finally, it is emphasized that cardiovascular disorders share an underlying RAS-related pathophysiology and that pharmacological RAS inhibitors increase ACE2 levels, which can increase entry of SARS-CoV-2 into the lungs and heart. RAS inhibition leads to ACE2 upregulation, which can render patients vulnerable to COVID-19, but it can also mitigate the toxic effects caused by virus-induced ACE2 downregulation, attenuating severe acute respiratory syndrome and myocarditis in patients with COVID-19[30].

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However, it is possible that the effect of RAS blockade in COVID-19 is conditional; in other words, if a patient has pre-existing RAS dysregulation associated with CVDs, the effect of RAS blockade may differ in the acute versus chronic setting[28]. Therefore, it is unclear whether RAS blockade would improve or exacerbate severity of the COVID-19 infection in patients with cardiovascular diseases.

Finally, it is noted that in mid-January 2021 the national vaccination campaign against COVID-19 was initiated in Brazil[12]. Thus, according to the expansion of vaccination for the general population, it is expected that different results from those presented in this study will be observed in relation to mortality due to COVID-19 in people with heart diseases.

Study limitations

This study has limitations such as the impossibility of analyzing the cases according to the severity classification of the clinical status of the pre-existing heart disease, as well as it was not possible to analyze whether the patients had other comorbidities, race/ethnicity and socioeconomic and environmental factors. It should be noted that these limitations are related to the diverse information made available in the database.

FINAL CONSIDERATIONS

The study identified an increased risk of mortality for people with heart diseases when compared to those without these diseases. Among individuals with heart diseases, adults aged between 21 and 50 years old were those with a higher risk of death. In addition to that, the study evidenced that female individuals over 51 years of age with heart diseases were at a lower risk of death when compared to male individuals belonging to the same age groups.

Faced with the presence of new variants of the SARS-CoV-2 virus, public health strategies aimed at confronting the COVID-19 pandemic must constantly monitor changes in the age profile of people considered at high risk, in addition to implementing measures that promote adherence to vaccination, in order to act effectively in reducing mortality among people with heart diseases.

REFERENCES

1. Organização Pan-Americana da Saúde [site de Internet]. Histórico da pandemia de COVID-19. 2021 [cited 2021 Set 7] Available from: https://www.paho.org/pt/COVID19/historico-da-pandemia-COVID-19.
2. Instituto Butantan [site de Internet]. Conheça os sintomas mais comuns da ômicron e de outras variantes da COVID-19. 2021 [cited 2022 Jan 21] Available from: https://butantan.gov.br/noticias/conheca-os-sintomas-mais-comuns-da-omicron-e-de-outras-variantes-da-COVID-19.
3. World Health Organization [site de Internet]. Clinical management of COVID-19: interim guidance. 2021 [cited 2021 Dez 3] Available from: https://iris.paho.org/handle/10665.2/52285.
4. Bae S, Kim SR, Kim MN, Shim WJ, Park SM. Impact of cardiovascular disease and risk factors on fatal outcomes in patients with COVID-19 according to age: a systematic review and meta-analysis. Heart. 2021 [cited 2022 Jan 17]; 107(5):373-80. DOI: http://dx.doi.org/10.1136/heartjnl-2020-317901.
5. Alsaied T, Aboulhosn JA, Cotts TB, Daniels CJ, Etheridge SP, Feltes TF, et al. Coronavirus Disease 2019 (COVID-19) pandemic implications in pediatric and adult congenital heart disease. J Am Heart Assoc. 2020 [cited 2022 Jan 21]; 9(12):e017224. DOI: https://doi.org/10.1161/JAHA.120.017224.
6. Instituto Brasileiro de Geografia e Estatística (IBGE) [site de Internet]. População. 2022 [cited 2022 Jan 3] Available from: https://cidades.ibge.gov.br/brasil/sp/panorama.
7. Fundação Sistema Estadual de Análise de Dados (SEADE) [site da Internet]. Boletim Completo. 2022 [cited 2022 Set 17]. Available from: https://www.seade.gov.br/coronavirus/.
8. Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Guia de vigilância epidemiológica: emergência de saúde pública de importância nacional pela doença pelo coronavírus 2019 – COVID-19. Ministério da Saúde; 2022 [cited 2022 Set 17]. Available from: https://www.gov.br/saude/pt-br/coronavirus/publicacoes-tecnicas/guias-e-planos/guia-de-vigilancia-epidemiologica-covid-19/view.
9. Wu L, O'Kane AM, Peng H, Bi Y, Motriuk-Smith D, Ren J. SARS-CoV-2 and cardiovascular complications: From molecular mechanisms to pharmaceutical management. Biochem Pharmacol. 2020 [cited 2022 Jan 21]; 178:114114. DOI: https://doi.org/10.1016/j.bcp.2020.114114.
10. Zheng YY, Ma YT, Zhang JY, Xie X. COVID-19 and the cardiovascular system. Nat Rev Cardiol. 2020 [cited 2022 Jan 25]; 17(5):259-60. DOI: https://doi.org/10.1038/s41569-020-0360-5.
11. Wu Z, McGoogan JM. Characteristics of and important lessons from the Coronavirus Disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. JAMA. 2020 [cited 2022 Jan 22]; 323(13):1239-42. DOI: https://doi.org/10.1001/jama.2020.2648.
12. Brasil. Ministério da Saúde. Departamento de Imunização e Doenças Transmissíveis. Plano Nacional de Operacionalização da Vacinação contra a COVID-19. Ministério da Saúde; 2022 [cited 2022 Set 17]. Available from: https://www.gov.br/saude/pt-br/coronavirus/vacinas/plano-nacional-de-operacionalizacao-da-vacina-contra-a-covid-19.

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13. Tsankov BK, Allaire JM, Irvine MA, Lopez AA, Sauvé LJ, Vallance BA, et al. Severe COVID-19 infection and pediatric comorbidities: a systematic review and meta-analysis. Int J Infect Dis. 2021 [cited 2022 Mar 12]; 103:246-56. DOI: https://doi.org/10.1016/j.ijid.2020.11.163.
14. Li N, Zhu L, Sun L, Shao G. The effects of novel coronavirus (SARS-CoV-2) infection on cardiovascular diseases and cardiopulmonary injuries. Stem Cell Res. 2021 [cited 2022 Mar 3]; 51:102168. DOI: https://doi.org/10.1016/j.scr.2021.102168.
15. Sachdeva S, Ramakrishnan S, Choubey M, Koneti NR, Mani K, Bakhru S, et al. Outcome of COVID-19-positive children with heart disease and grown-ups with congenital heart disease: a multicentric study from India. Ann Pediatr Cardiol. 2021 [cited 2022 Jan 29]; 14(3):269-77. DOI: https://doi.org/10.4103/apc.apc_134_21.
16. Carlucci L, D'Ambrosio I, Balsamo M. Demographic and attitudinal factors of adherence to quarantine guidelines during covid-19: the italian model. Front Psychol. 2020 [cited 2022 Fev 18]; 11:559288. DOI: https://doi.org/10.3389/fpsyg.2020.559288.
17. Banho CA, Sacchetto L, Campos GRF, Bittar C, Possebon FS, Ullmann LS, et al. Effects of SARS-CoV-2 P.1 introduction and the impact of COVID-19 vaccination on the epidemiological landscape of São José Do Rio Preto, Brazil. Med Rxiv. 2021. Preprint [cited 2022 Mar 16]. DOI: https://doi.org/10.1101/2021.07.28.21261228.
18. Instituto Butantan [site da Internet]. Seis fatos sobre a ômicron, a variante mais transmissível da COVID-19. [cited 2022 Fev 17] Available from: https://butantan.gov.br/noticias/seis-fatos-sobre-a-omicron-a-variante-mais-transmissivel-da-COVID-19.
19. Governo do Estado de São Paulo [site da Internet]. Sobe 61% o número de crianças e adolescentes em UTI por COVID-19 no estado de SP. [cited 2022 Fev 29]. Available from: https://www.saopaulo.sp.gov.br/noticias-coronavirus/sobe-61-o-numero-de-criancas-e-adolescentes-em-uti-por-COVID-19-no-estado-de-sp/.
20. Governo de Santa Catarina [site da Internet]. Internações de crianças com COVID-19 em UTIs aumentam 400% em 15 dias em Santa Catarina. [cited 2022 Fev 28]. Available from: https://www.sc.gov.br/noticias/temas/saude/internacoes-de-criancas-com-COVID-19-em-utis-aumentaram-400-em-15-dias-em-sc.
21. Governo do Estado de São Paulo [site da Internet]. #VacinaJá. [cited 2022 Dez 15] Available from: https://www.vacinaja.sp.gov.br/.
22. Peckham H, Gruijter NM, Raine C, Radziszewska A, Ciurtin C, Wedderburn LR, et al. Male sex identified by global COVID-19 meta-analysis as a risk factor for death and ITU admission. Nat Commun. 2020 [cited 2022 Fev 27]; 11(1):6317. DOI: https://doi.org/10.1038/s41467-020-19741-6.
23. Klein SL, Dhakal S, Ursin RL, Deshpande S, Sandberg K, Mauvais-Jarvis F. Biological sex impacts COVID-19 outcomes. PLoS Pathog. 2020 [cited 2022 Jan 17]; 16(6):e1008570. DOI: https://doi.org/10.1371/journal.ppat.1008570.
24. Karlberg J, Chong DS, Lai WY. Do men have a higher case fatality rate of severe acute respiratory syndrome than women do? Am J Epidemiol. 2004 [cited 2022 Jan 20]; 159(3):229-31. DOI: https://doi.org/10.1093/aje/kwh056.
25. Flanagan KL, Fink AL, Plebanski M, Klein SL. Sex and gender differences in the outcomes of vaccination over the life course. Annu Rev Cell Dev Biol. 2017 [cited 2022 Fev 11]; 33:577-99. DOI: https://doi.org/10.1146/annurev-cellbio-100616-060718.
26. Esme M, Koca M, Dikmeer A, Balci C, Ata N, Dogu BB, et al. Older adults with coronavirus disease 2019: a nationwide study in Turkey. J Gerontol A Biol Sci Med Sci. 2021 [cited 2022 Jan 6]; 76(3):e68-e75. DOI: https://doi.org/10.1093/gerona/glaa219.
27. Mueller AL, McNamara MS, Sinclair DA. Why does COVID-19 disproportionately affect older people? Aging (Albany NY). 2020 [cited 2022 Fev 14]; 12(10):9959-81. DOI: https://doi.org/10.18632/aging.103344.
28. Hanff TC, Harhay MO, Brown TS, Cohen JB, Mohareb AM. Is There an association between COVID-19 mortality and the renin-angiotensin system? A call for epidemiologic investigations. Clin Infect Dis. 2020 [cited 2022 Jan 6]; 71(15):870-4. DOI: https://doi.org/10.1093/cid/ciaa329.
29. Emadi-Baygi M, Ehsanifard M, Afrashtehpour N, Norouzi M, Joz-Abbasalian Z. Corona Virus Disease 2019 (COVID-19) as a system-level infectious disease with distinct sex disparities. Front Immunol. 2021 [cited 2022 Fev 27]; 12:778913. DOI: https://doi.org/10.3389/fimmu.2021.778913.
30. Chang WT, Toh HS, Liao CT, Yu WL. Cardiac involvement of COVID-19: a comprehensive review. Am J Med Sci. 2021 [cited 2022 Fev 23]; 361(1):14-22. DOI: https://doi.org/10.1016/j.amjms.2020.10.002.