COVID-19 hospitalization and death and relationship with social determinants of health and morbidities in Espírito Santo State, Brazil: a cross-sectional study

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Abstract

Objective: To analyze the association between social determinants and morbidities for the outcomes of hospitalization, intensive care unit admission and death by COVID-19 in Espírito Santo State, Brazil. **Methods:** Cross-sectional study with secondary data from confirmed cases of COVID-19, reported in the Notifiable Diseases Information System. Poisson regression was used to estimate the prevalence ratios. **Results:** 104,384 cases reported between February 28th and September 1st, 2020 were studied. The outcomes under study were more frequent among male, elderly, yellow, followed by black, uneducated and with multimorbidity. There was a higher risk of death among people over the age of 60 (PR=56.31 – 95%CI 34.24;92.61), multimorbidities (PR=3.63 – 95%CI 3.16;4.17), kidney disease (PR=3.42 – 95%CI 2.81;4.15) and neoplasms (PR=3.15 – 95%CI 2.41;4.13). **Conclusion:** The effect of social determinants and morbidities on hospitalization and deaths by COVID-19 is evident.

Keywords: Coronavirus Infections; Hospitalization; Mortality; Social Determinants of Health; Cross-Sectional Studies.

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Introduction

The year 2020 was marked by the worldwide spread of SARS-CoV-2, the virus that causes COVID-19, which was declared a pandemic disease by the World Health Organization (WHO).[1] The speed with which transmission of the virus occurs has been evidenced in the growth and magnitude of cases reported worldwide. According to WHO data, by November 19th, 2020, some 55 million people had become infected and more than 1.3 million had died as a result of COVID-19. In Brazil, during the same period, there had been more than 5.9 million people infected and 168 thousand deaths.[2] In the Espírito Santo state in particular there had been 175,300 confirmed cases, 4,082 deaths and the fatality rate was estimated at 2.4%.[3]

> *Understanding how social determinants of health can negatively influence the outcomes of COVID-19, together with knowledge about the form of exposure to these determinants, allow Public Health policies to consider risks made greater by comorbidities.*

Although initially, the virus causes mild respiratory illness, this infection can lead to severe respiratory syndrome. These severe forms of COVID-19 are more likely to develop in elderly people and in those with previous chronic diseases.[4] A study conducted in Brazil about comorbidities in people over 50 years old found 67.8% prevalence of individuals with two diseases or more, and 47.1% with three or more, accounting for 26 million and 18 million Brazilians, respectively.[5] These are people who would be at greater risk of serious outcomes if they became infected with SARS-CoV-2.

Most diseases arise from the situations in which one is born, lives, studies, works, and even plays. This set of conditions, identified as the 'social determinants of health' and which are primarily responsible for generating systematic differences across population groups, are at the core of health inequalities.[6] In the context of profound social problems in Brazil, it is difficult to discuss health issues without considering the inequalities present in the country, and their reflections are evident in living and housing conditions.

In the face of the new coronavirus pandemic, an important relationship between multimorbidity, COVID-19, and social determinants has been observed, with individuals with poorer socioeconomic conditions being the most affected.[7] The prevalence and severity of COVID-19 are closely linked to other incident morbidities, especially among the poorest, least educated, and those with least access to health services.

Understanding how social determinants of health can negatively influence the outcomes of COVID-19, together with knowledge about the form of exposure to these determinants, allow Public Health policies to consider risks made greater by comorbidities, so that, among their coordinated actions, they also and in particular address those at greater risk and with less visibility and protection.

This study aimed to analyze association between social determinants and morbidities, and COVID-19 'hospitalization', 'intensive care unit (ICU) admission' and 'death' outcomes in the state of Espírito Santo state, in Southeastern Brazil.

Methods

This is a cross-sectional analytical study of secondary data based on information on confirmed COVID-19 cases in Espírito Santo state, available on the Notifiable Health Conditions Information System.

Espírito Santo is the smallest state in the Southeast region of Brazil, with an estimated population of 4,018,650 inhabitants[8] and its economy is mostly based on the services sector. The age structure of the state's population is undergoing intense transformation: 13.55% are over 60 years old and life expectancy is 78.8 years, according to projections for 2020.[9] The regional healthcare network has undergone intense adaptations to meet COVID-19-related demands. In November 2020, its installed capacity was 1,532 beds, divided between 715 ICU beds and 817 ward beds.[10]

We analyzed all cases of COVID-19 in Espírito Santo state confirmed by laboratory tests or clinical-epidemiological diagnostic criteria. All cases, from the first case notified on February 28th, 2020, to the last case recorded on September 1st, 2020, were followed up for 15 days to assess outcomes in this period.

The database used was made available by the Espírito Santo State Health Department and was derived from the online system for compulsory notification of cases. During the notification process, socio-demographic information, information on individual symptoms and pre-existing morbidities as well as follow-up data for each case are collected.

The study outcomes were COVID-19 'hospitalization', 'ICU admission' and 'death' (yes; no). The independent variables were:

a) Sex (female; male);

b) Race/skin color (white; black; brown [mixture of two or more races/skin colors]; yellow [people of Asian origin]; indigenous);

c) Age (complete years: 18-29; 30-39; 40-49; 50-59; 60 or over);

d) Schooling (no schooling; complete elementary education; complete high school education; complete higher education and above);

e) Presence of morbidities (none; one; multimorbidity [≥2 morbidities]).

As the study used secondary data, the completeness of the independent variable data was assessed. The following morbidities were selected:

a) Pre-existing lung disease;

b) Cardiovascular disease;

c) Chronic kidney disease;

d) Chronic liver disease;

e) Diabetes *mellitus*;

f) HIV infection;

g) Obesity;

h) Tuberculosis;

i) Chronic neurological disease;

j) Neoplasms.

However, pre-existing lung diseases, neoplasms, cardiovascular disease, neurological disease, kidney disease, diabetes *mellitus*, tobacco smoking, obesity, and HIV infection were evaluated separately. Morbidities such as tuberculosis, liver disease, and other immunodeficiencies (except HIV infection) could not be assessed separately, given the small number of reported cases. All conditions were estimated based on the report given by the notified individual, the report of a family member, or identification by the professional in charge of the care, as in the case of obesity, for instance.

The data were organized using Excel and then analyzed using the Stata 13.0 statistical program.

Since this was a study based on secondary data, the completeness (percentage of filled-in fields) of the independent variables was assessed. The analysis was carried out in multiple steps taking a 5% significance level. First, the frequency of the independent variables (sex; race/skin color; age; schooling; presence of morbidities) and their association with the outcomes under study was verified using Pearson's chi-square test. In the second step, possible association between the exposures (independent variables) and outcomes (hospitalization; ICU admission; death) was verified by means of Poisson regression with robust variance, calculation of crude prevalence ratios and respective 95% confidence intervals (95%CI).

Finally, multivariate analysis was performed, in which variables that had a p-value <0.2 in the crude analysis were considered as potential confounding factors and were therefore only included in the model once, adopting a p-value <0.05 for the final result. When assessing the quality of the fit of each model, the Hosmer & Lemeshow test was used after each Poisson regression in those situations in which, for all models presented, the test statistic was not significant, i.e. p>0.05 and, therefore, the fit was considered adequate. The chi-square test for linear trend was used with a 5% significance level to assess the possibility of a dose-response effect between ordinal categorical exposure variables and the probability of the outcomes under study.

For all associations between exposures and outcomes, the sample power was calculated using the OpenEpi statistical program, version 3.01, taking as parameters a 95% confidence interval (95%CI) and a minimum prevalence ratio of 1.2. The association with the lowest power was 'HIV infection and risk of death from COVID-19', equal to 78.61%.

The study project was submitted to the Human Research Ethics Committee of the Federal University of Espírito Santo Health Sciences Center, and approved as per Opinion No. 4.036.052, issued on May 19th, 2020.

Results

A total of 104,384 cases of COVID-19 confirmed in the state of Espírito Santo state were investigated. Regarding completeness, the 'sex' and 'age' variables were the most complete, with 99.98% and 100.00% of information respectively, followed by

'presence of morbidity' (98.80%), 'race/skin color' (81.33%) and 'schooling' which had the poorest completeness (68.15%).

Most participants were female (53.09%), were of white (42.25%) and brown (41.23%) race/skin color, aged between 30 and 49 years (48.33%), and had complete high school education (44.46%); 18.17% had a pre-existing morbidity, and 8.47% had multimorbidity (Table 1).

Hospitalizations due to COVID-19 were more frequent among males (9.93%) and people of yellow race/skin color (10.32%). Hospitalization prevalence increased with age, ranging from 1.60% in individuals aged 18 to 29 years to 27.35% among those aged 60 years or older (Table 1). An inverse relationship was seen in the schooling categories, with higher hospitalization prevalence among individuals who reported lower levels of schooling. Hospitalization prevalence among individuals with just one morbidity was 12.99%; and 28.32% for those with multimorbidity, whereas for people without morbidities hospitalization prevalence was 4.17% (Table 1).

ICU admissions followed the same pattern as hospitalizations for the exposure variables, being more frequent among individuals of the male sex (5.87%), those of yellow race/skin color (7.31%), those aged 60 or older (18.37%), those with no schooling (7.75%) and those with multimorbidity (18.18%) (Table 1).

Regarding COVID-19 deaths among the reported cases, deaths were more frequent among males (3.85%), compared to females (2.63%); prevalence of death was 4.88% for people of yellow race/skin color, and 3.44% for people of white race/skin color, (Table 1). The highest proportion of deaths by age categories was found among people aged 60 or older (19.17%), while in relation to schooling, the highest proportion of deaths corresponded to those with no schooling (7.34%). The proportion of deaths in individuals with multimorbidity was 15.79%, 5.65% in those with only one morbidity and 1.12% in cases with no morbidities (Table 1).

Table 2 presents the crude and adjusted prevalence ratios for the three outcomes, according to sociodemographic characteristics and morbidities. Being female was negatively associated with all three outcomes (hospitalizations, ICU admissions, and death). After adjustment, being female reduced the likelihood of being hospitalized due to COVID-19 by 33% (PR=0.67 - 95%CI 0.62;0.71) compared to males; the reduction in the likelihood of a female being admitted to an ICU due to COVID-19 was 38% (PR=0.62 - 95%CI 0.56;0.69), while there was a 37% reduction in the likelihood of death (PR=0.63 - 95%CI 0.57;0.70) compared to males (Table 2).

Individuals of yellow race/skin color were 35% (95%CI 1.19;1.52) more likely (95%CI 1.19;1.52) to be hospitalized, and 81% (95%CI 1.52;2.16) were more likely to be admitted to an ICU than those of white race/skin color. Being of yellow race/skin color was also associated with a 27% (95%CI 1.08;1.50) increase in the likelihood of dying from COVID-19, compared to those of white race/skin color. Individuals of black race/skin color, in turn, had a 28% higher probability (95%CI 1.13;1.44) of being hospitalized, and a 34% increase (95%CI 1.11;1.62) in the probability of being hospitalized in an ICU, compared to those of white race/skin color. With regard to COVID-19 deaths, the probability of people of yellow race/skin color was 22% higher (95%CI 1.03;1.45), when compared to those of white race/skin color (Table 2).

The three outcomes studied showed an inverse relationship with schooling categories. Lower levels of schooling had higher odds of a negative COVID-19-related outcome. Individuals with no schooling showed a 78% and 108% increase in the likelihood of being hospitalized and being admitted to an ICU, respectively, compared to individuals with complete higher education (Table 2). As for deaths, having no schooling was associated with a 3.35-fold (95%CI 2.63;4.26) increase in the likelihood of dying from COVID-19, in relation to those with higher education (Table 2).

The probability of a negative outcome increased as age increased: the probability of being hospitalized was 11.39 times higher among individuals aged 60 years or older compared with those aged 18 to 29 years, while being 60 years or older was associated with a 10.70-fold increase in the probability of being admitted to an ICU compared with the youngest stratum (Table 2). When death was assessed, the prevalence ratio was 56.31 (95%CI 34.24;92.61) for those aged 60 years or older compared with those aged 18 to 29 years (Table 2).

Having a single morbidity increased the likelihood of being hospitalized by 49% (95%CI 1.36;1.64); and having multimorbidity was associated with a 2.66-fold

Table 1 – Frequencies of sociodemographic charateristics and morbidities, overall and stratified by negative health outcomes, Espírito Santo state, Brazil, 2020

Exposure variable	N	%	Hospitalization n (%)[a] Yes p<0.001[b]	ICU[c] n (%)[a] Yes p<0.001[b]	Death n (%)[a] Yes p<0.001[b]
Sex (104,359)					
Female	55,401	53.09	2,794 (7.10)	1,292 (4.14)	1,363 (2.63)
Male	48,958	46.91	3,476 (9.93)	1,653 (5.87)	1,764 (3.85)
Race/skin color (81,338)					
White	34,366	42.25	1,972 (7.59)	909 (4.53)	1,106 (3.44)
Black	6,253	7.69	468 (9.79)	231 (5.91)	251 (4.27)
Yellow	7,018	8.63	553 (10.32)	310 (7.31)	324 (4.88)
Brown	33,536	41.23	2,127 (8.58)	995 (4.99)	1,094 (3.55)
Indigenous	165	0.20	7 (5.56)	2 (1.85)	3 (2.00)
Age (years) (104,384)					
18-29	19,603	18.78	222 (1.60)	55 (0.94)	27 (0.37)
30-39	27,566	26.41	527 (2.75)	143 (1.55)	71 (0.60)
40-49	22,885	21.92	842 (5.14)	250 (3.07)	144 (1.45)
50-69	16,514	15.82	1,086 (9.22)	380 (6.42)	267 (3.67)
≥60	17,816	17.07	3,595 (27.35)	1,309 (18.37)	1,575 (19.17)
Schooling (68,152)					
No schooling	13,127	19.26	1,395 (13.39)	650 (7.75)	893 (7.34)
Elementary education	9,642	14.15	562 (7.51)	244 (4.17)	308 (3.44)
High school education	30,298	44.46	910 (3.88)	353 (1.93)	300 (1.06)
Higher education	15,085	22.13	394 (3.33)	142 (1.59)	82 (0.58)
Morbidity (103,136)					
None	75,661	73.36	2,155 (4.17)	858 (2.12)	790 (1.12)
One morbidity	18,741	18.17	1,978 (12.99)	926 (7.47)	988 (5.65)
Multimorbidity	8,734	8.47	2,053 (28.32)	1,121 (18.18)	1,295 (15.79)

a) Includes subjects with both variable fields filled in; b) Pearson's chi-square test; c) ICU: intensive care unit.

(95%CI 2.43;2.93) increase in the same outcome, compared to individuals with no morbidities. In the case of ICU admissions, this increase was 65% (95%CI 1.42;1.92) among those with one morbidity and 3.09 times greater (95%CI 2.65;3.60) in individuals with multimorbidity. Having a morbidity increased the likelihood of dying from COVID-19 by 78% (95%CI 1.54;2.05), while having multimorbidity increased the likelihood 3.63-fold (95%CI 3.16;4.17) compared to not having a morbidity (Table 2).

The trend analyses suggested a linear effect between the 'age', 'schooling' and 'morbidity' variables and the outcomes studied. In the case of the 'age' variable, prevalence of hospitalizations, ICU admissions and deaths increased significantly as age increased (p<0.001); the same occurred with the 'morbidity' variable, the outcome prevalence rates of which increased as the number of morbidities increased (p<0.001). In the case of the 'schooling' variable, the outcome probabilities were inversely proportional,

Table 2 – Crude and adjusted prevalence ratios (PR) and respective 95% confidence intervals (95%CI) for COVID-19 hospitalizations, hospitalizations in intensive care unit (ICU) and deaths, according to morbidity and sociodemographic characteristics, Espírito Santo state, Brazil, 2020

Variable	Crude analysis			Adjusted analysis		
	Hospitalization PR (95%CI)	ICU admission PR (95%CI)	Death PR (95%CI)	Hospitalization PR (95%CI)	ICU admission PR (95%CI)	Death PR (95%CI)
Morbidity[a]						
None	1.00	1.00	1.00	1.00	1.00	1.00
One morbidity	3.11 (2.93;3.29)	3.53 (3.22;3.86)	5.06 (4.62;5.55)	1.49 (1.36;1.64)	1.65 (1.42;1.92)	1.78 (1.54;2.05)
Multimorbidity	6.78 (6.42;7.16)	8.59 (7.89;9.35)	14.15 (12.99;15.41)	2.66 (2.43;2.93)	3.09 (2.65 - 3.60)	3.63 (3.16;4.17)
Chi-square trend	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Sex[b]						
Male	1.00	1.00	1.00	1.00	1.00	1.00
Female	0.71 (0.68;0.75)	0.70 (0.65;0.75)	0.68 (0.63;0.73)	0.67 (0.62;0.71)	0.62 (0.56;0.69)	0.63 (0.57;0.70)
Race/skin color[c]						
White	1.00	1.00	1.00	1.00	1.00	1.00
Black	1.28 (1.17;1.41)	1.35 (1.13;1.50)	1.24 (1.08;1.42)	1.28 (1.13;1.44)	1.34 (1.11;1.62)	1.22 (1.03;1.45)
Yellow	1.35 (1.24;1.48)	1.61 (1.42;1.82)	1.42 (1.25;1.60)	1.35 (1.19;1.52)	1.81 (1.52;2.16)	1.27 (1.08;1.50)
Brown	1.12 (1.06;1.19)	1.10 (1.01;1.20)	1.03 (0.95;1.12)	1.17 (1.08;1.26)	1.21 (1.07;1.37)	1.11 (0.99;1.23)
Indigenous	0.73 (0.35;1.50)	0.40 (0.10;1.61)	0.58 (0.18;1.78)	0.52 (0.17;1.59)	0.76 (0.19;2.95)	0.80 (0.20;3.12)
Schooling[d]						
Higher education	1.00	1.00	1.00	1.00	1.00	1.00
High school education	1.16 (1.03;1.30)	1.21 (1.00;1.47)	1.84 (1.44;2.34)	1.19 (1.06;1.35)	1.28 (1.04;1.59)	1.71 (1.33;2.20)
Elementary education	2.25 (1.99;2.55)	2.63 (2.14;3.22)	5.95 (4.67;7.59)	1.51 (1.31;1.73)	1.74 (1.38;2.18)	2.76 (2.14;3.56)
No schooling	4.02 (3.60;4.48)	4.88 (4.08;5.84)	12.72 (10.16;15.93)	1.78 (1.58;2.02)	2.08 (1.69;2.56)	3.35 (2.63;4.26)
Chi-square trend	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Age (years)[e]						
18-29	1.00	1.00	1.00	1.00	1.00	1.00
30-39	1.71 (1.47;2.00)	1.65 (1.27;2.13)	1.98 (1.32;2.97)	1.64 (1.34;2.02)	1.72 (1.20;2.46)	2.07 (1.16;3.67)
40-49	3.31 (2.77;3.72)	3.16 (2.48;4.02)	5.78 (3.99;8.38)	2.89 (2.38;3.51)	2.69 (1.91;3.78)	5.39 (3.18;9.11)
50-59	5.76 (5.00;6.64)	6.99 (5.54;8.80)	14.60 (10.19;20.92)	4.38 (3.61;5.30)	4.23 (3.88;7.49)	11.39 (6.83;18.99)
≥60	17.10 (14.96;19.54)	21.33 (17.12;26.57)	83.49 (58.94;118.26)	11.39 (9.49;13.68)	10.70 (10.34;19.48)	56.31 (34.24;92.61)
Chi-square trend	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

a) Analysis adjusted for sex, race/skin color, schooling and age; b) Analysis adjusted for morbidity, race/skin color, schooling and age; c) Analysis adjusted for morbidity, sex, schooling and age; d) Analysis adjusted for morbidity, sex, race/skin color and age; e) Analysis adjusted for morbidity, sex, race/skin color and schooling.

and prevalence of COVID-19 hospitalizations, ICU admissions and deaths increased as level of schooling decreased (p<0.001).

Table 3 presents the risks of unfavorable outcomes according to the morbidities reported, after analysis adjusted for potential confounding factors. All morbidities were significantly associated with higher risks of hospitalization, ICU admission and death, with HIV infection (PR=2.40 - 95%CI 1.26;4.57), neoplasms (PR=3.15 - 95%CI 2.41;4.13) and kidney disease (PR=3.42 - 95%CI 2.81;4.15) leading to higher risk of death from COVID-19.

Discussion

The results of the study revealed that advanced age (60 years or more), male sex, low schooling, yellow and black race/skin color, presence of morbidity and

Table 3 – Crude and adjusted prevalence ratios (PR) and respective 95% confidence intervals (95%CI) for COVID-19 hospitalizations, hospitalizations in intensive care unit (ICU) and deaths, according to morbidity, segundo morbidity, Espírito Santo state, Brazil, 2020

Morbidity	N (%)	Crude analysis			Adjusted analysis[a]		
		Hospitalization PR (95%CI)	ICU admission PR (95%CI)	Death PR (95%CI)	Hospitalization PR (95%CI)	ICU admission PR (95%CI)	Death PR (95%CI)
Lung disease							
No	100,093 (96.87)	1.00	1.00	1.00	1.00	1.00	1.00
Yes	3,235 (3.13)	2.28 (2.10;2.48)	2.47 (2.19;2.79)	3.13 (2.79;3.52)	1.86 (1.65;2.09)	2.02 (1.68;2.43)	2.01 (1.70;2.36)
Neoplasms							
No	102,966 (99.65)	1.00	1.00	1.00	1.00	1.00	1.00
Yes	363 (0.35)	5.29 (4.85;5.78)	3.49 (2.93;4.17)	8.89 (7.88;10.04)	2.76 (2.23;3.41)	1.72 (1.10;2.68)	3.15 (2.41;4.13)
Cardiovascular disease							
No	83,249 (80.55)	1.00	1.00	1.00	1.00	1.00	1.00
Yes	20,100 (19.45)	3.56 (3.40;3.73)	4.37 (4.07;4.69)	5.92 (5.52;6.35)	1.16 (1.07;1.26)	1.34 (1.18;1.52)	1.36 (1.21;1.52)
Kidney disease							
No	102,555 (99.23)	1.00	1.00	1.00	1.00	1.00	1.00
Yes	793 (0.77)	5.85 (5.38;6.36)	6.45 (5.67;7.34)	9.46 (8.38;10.67)	2.81 (2.41;3.27)	2.90 (2.28;3.69)	3.42 (2.81;4.15)
Diabetes *mellitus*							
No	95,523 (92.44)	1.00	1.00	1.00	1.00	1.00	1.00
Yes	7,810 (7.56)	3.82 (3.63;4.02)	4.65 (4.33;5.00)	6.02 (5.61;6.47)	1.73 (1.60;1.88)	2.04 (1.81;2.30)	2.07 (1.86;2.30)
Tobacco smoking							
No	101,424 (98.16)	1.00	1.00	1.00	1.00	1.00	1.00
Yes	1,905 (1.84)	2.68 (2.44;2.96)	3.13 (2.74;3.58)	3.40 (2.95;3.91)	1.72 (1.50;1.97)	1.94 (1.59;2.38)	1.72 (1.42;2.08)
Obesity							
No	99,268 (96.18)	1.00	1.00	1.00	1.00	1.00	1.00
Yes	3,940 (3.82)	2.00 (1.85;2.18)	1.96 (1.73;2.22)	2.48 (2.20;2.79)	1.81 (1.62;2.02)	1.72 (1.44;2.06)	2.03 (1.74; 2.36)
HIV infection							
No	103,126 (99.80)	1.00	1.00	1.00	1.00	1.00	1.00
Yes	209 (0.20)	3.39 (2.66;4.32)	3.44 (2.39;4.97)	2.93 (1.88;4.56)	3.18 (2.28;4.43)	3.34 (1.98;5.62)	2.40 (1.26;4.57)
Neurological diseases							
No	102,495 (99.19)	1.00	1.00	1.00	1.00	1.00	1.00
Yes	839 (0.81)	4.44 (4.01;4.92)	4.15 (3.52;4.89)	7.50 (6.57;8.57)	1.96 (1.64;2.34)	1.41 (1.02;1.96)	2.38 (1.92;2.94)

a) Adjusted for sex, race/skin color, age and schooling.

multimorbidity were conditions associated with a higher risk of COVID-19 hospitalizations, ICU admissions and mortality, while being female showed a protective effect. Two recent systematic reviews found strong evidence of association between the male sex, advanced age and comorbidities and COVID-19 severity and poorer prognosis.[4,11]

As in other studies, the probability of negative outcomes related to COVID-19, with risk of death, was greater for the male sex.[12,13] Lower risk of mortality among females has also been reported in Italy.[14] To date, it is believed that differences between males and females with regard to levels and types of circulating sex hormones may influence susceptibility to SARS-CoV-2 infection. A previous study has shown that sex hormones modulate adaptive and innate immune responses.[13]

Lower fatality and lower other negative outcomes may be associated with greater awareness of the symptoms of the disease and seeking health services

more quickly, in the case of female sex. Male people tend to seek health care services only in the most severe phases of the disease, when therapeutic resources are generally fewer.[12,15]

Although COVID-19 was initially considered a great equalizer, requiring physical distancing measures all over the world, it is increasingly being shown that social inequalities with regard to health impact morbidity and mortality of this disease.[16] In the United States, the SARS-CoV-2 infection rate is three times higher in predominantly Black counties compared to predominantly White counties; and the mortality rate is six times higher.[17] Greater risk of hospitalization, ICU admission and death were identified in people of black, brown and yellow skin color. This difference was not found in indigenous people, probably because of the small number of people classified in this group.

A study in the United Kingdom showed that with regard to age-matched control, Blacks were 4.3 times more likely to die from COVID-19 than Whites. These data also show that, compared to Whites, Bangladeshis, Pakistanis, Indians, and people of mixed ethnicities are at higher risk of dying from COVID-19.[18]

The social determinants underlying the health conditions affecting these populations are believed to make them more vulnerable to the virus. These determinants include, but are not limited to, reduced access to health care, economic insecurity, poor neighborhood and housing conditions, and reduced availability of resources.[19]

Race and ethnicity, in turn, are inextricably linked to socioeconomic position. Self-declared non-Whites are disproportionately represented in social segments with lower income or less education.[20] Lower income and lower educational level result in poorer housing conditions, less ability to buy healthy food, jobs with lower wages, and poorer access to health care, among other situations that affect the transmission of COVID-19 and its complications.

This study found higher prevalence of negative outcomes among individuals of black/yellow/brown/ indigenous race/skin color and among those in the lowest categories of schooling. This strongly reinforces the argument that determinants of health should be at the center of policies to address COVID-19. Physical distancing measures, necessary to prevent the spread of COVID-19, are substantially more difficult for those whose social determinants are more adverse.[16] Also, many who cannot work from home often rely on public transport to get to work, further increasing the risk of SARS-CoV-2 transmission.[20] A study by Baqui et al.,[7] also conducted in Brazil, demonstrated that the 'ethnicity' factor (for example, being of black or brown race/skin color) is the second most important risk factor for mortality as an outcome, second only to the 'age' factor, thus reinforcing the relevance of social determinants.

This study found higher probabilities of negative health outcomes in relation to advancing age. These findings are partially in agreement with a previous review.[21] A recent meta-analysis confirmed that advanced age (65 years) was associated with death in individuals with COVID-19.[13,22] In Brazil, it is estimated that at least 34 million individuals aged 50 years or older have some type of morbidity associated with risk of developing clinically severe forms of COVID-19.[23]

A meta-analysis,[11] indicated that the presence of comorbidities leads to an increased risk of developing serious events in people infected with SARS-CoV-2, i.e. ICU admission, intubation, and mortality. A further meta-analysis,[24] this time on the impact of cardiovascular disease in cases of COVID-19, found that hypertension and cerebro-cardiovascular disease had a statistically significant impact on ICU admission.

A study conducted in China found that individuals with at least one comorbidity were older (mean age 60.8 years *versus* 44.8 years) and having at least one comorbidity was more commonly seen in severe cases compared to non-severe cases (32.8% *versus* 10.3%). In addition, individuals with multimorbidity had significantly higher risks of having a negative outcome (ICU admission, invasive ventilation, or death) compared with those who had just one comorbidity; and even higher risk when compared to those who did not have any comorbidities.[25]

As presented in this study, people with chronic diseases are at increased risk of unfavorable outcomes due to COVID-19, even after controlling for potential confounding factors such as age, sex, and schooling. The evidence so far points to a significantly higher risk of complications and death from COVID-19 in people with certain morbidities. A study of registered cases in

China showed that the overall fatality of the disease was 2.3%, higher among groups of people with pre-existing morbidities: 10.5% for cardiovascular disease, 7.3% for diabetes *mellitus*, 6.3% for chronic respiratory disease, 6.0% for hypertension, and 5.6% for neoplasms.[26]

Obesity was not studied as a potential factor in COVID-19 complications in the first studies conducted, but was rather a hypothesis taken into consideration later.[26,27] In China, among 383 individuals analyzed, overweight was associated with an 86% increased risk and obesity with a 142% increased risk of developing severe pneumonia compared with individuals with normal body mass index (BMI), even after controlling for potential confounding factors.[28] A study conducted with 4,103 North American subjects showed that having BMI>40kg/m^2 was the second strongest independent predictor of hospitalization, after old age.[29] Having BMI>35kg/m^2 was also associated with increased chances of invasive mechanical ventilation, regardless of other comorbidities.[30]

Provided it is backed by evidence, careful medical history investigation during screening of individuals with COVID-19 should be prioritized, contributing to the identification of those most likely to develop serious adverse COVID-19 outcomes. Greater attention should be paid to individuals with COVID-19 who had comorbidities when diagnosis was confirmed. Identifying these individuals may help in stratification by the highest risk level, allowing for a targeted and specific approach to preventing fatal events.[11] The findings of this study show how weak the Brazilian National Health System (SUS) still is in adequately addressing social inequalities with regard to health. Despite progress in recent years, the persistent social and geographical inequalities in access to and use of SUS services tend to impact health outcomes in the most vulnerable populations, especially in pandemic situations.

This study is based on a large number of observations; however, it has limitations, many of them inherent to research using secondary data, such as the possibility of form-filling errors and missing information. Underreporting of comorbidities, possibly attributable to lack of knowledge or unavailability of diagnostic tests, may favor overestimation of the strength of association with negative outcomes, since in severe cases, this information is usually more complete. Another limitation of this study refers to its data not being linked to the Mortality Information System and, therefore, the possibility of underreporting should be considered. Finally, the study had a time limit for collection of data on the outcome 15 days after the date of notification, and many outcomes, especially death, can occur with a longer time interval. However, this is non-differential bias, because there is no theoretical basis or evidence that time interval between notification and outcome is different among different population groups.

Social determinants of health should be included among the priorities for research on the pandemic and, in a broader sense, should be addressed when defining Public Health objectives and implementing public health policy. Understanding how social determinants of health contribute to incidence, prevalence, treatment, and mortality associated with COVID-19 may help in the development of more effective interventions to mitigate transmission of this disease.

Authors' contributions

Mascarello KC contributed to the concept of the study, performing the analyses, and drafting the manuscript. Vieira ACBC contributed to drafting the manuscript. De Souza ASS, Marcarini WD, Barauna VG and Maciel ELN contributed to the concept of the study and drafting the manuscript. All the authors have approved the final version of the manuscript and are responsible for all aspects thereof, including the guarantee of its accuracy and integrity.

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