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# Hierarchy of Covid-19-Related Flu Symptoms According to Sex and Color or Race in Reports of Patients with Severe Acute Respiratory Syndrome in Brazil

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### Authors' contributions

This work was carried out in collaboration between both authors. Author JFSS designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Author DDS managed the literature searches. Both authors read and approved the final manuscript.

#### Article Information

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## ABSTRACT

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The COVID-19 is a disease that presents a wide variety of combinations and intensities of symptoms, characteristic of a Flu Syndrome (FS), which can quickly evolve to a Severe Acute Respiratory Syndrome (SARS). The objectives of this study were to evaluate the hierarchy of symptoms of FS in patients with SARS caused by COVID-19 and to develop a prediction model for potential cases based on sex and race. Binary logistic regression modeling was used in 405,419 records selected from the database of the Ministry of Health of Brazil. It was found that men were more affected by the disease, with a 15.5% higher risk than women. They also died more, with a 13.8% and 15% higher risk for all causes and for COVID-19, respectively. The chances of more than one non-white patient dying from all causes ranged from 18.4% to 38.7% and for Covid-19 it

ranged from 16.7% to 64.3% according to race. Fever, muscle pain and loss of smell or taste alternate in the first three positions of the symptom hierarchy, according to sex and race. Cough was only relevant for white men and sore throat for black men. Vomiting was only relevant for black women. The best prediction model developed encompassed seven symptoms adjusted for age, sex and race, but was able to explain only 63% of the cases of COVID-19. Possibly racial diversity, and the socioeconomic inequality associated with it, make the challenge of estimating probabilities of infection by COVID-19, based on symptoms, more complicated in Brazil than in other countries.

Keywords: Black; COVID-19; disparity; race; sex.

## 1. INTRODUCTION

The Flu Syndrome (FS) is a condition characterized by the sudden appearance of signs and symptoms that include pain (head, throat, muscle, joint and abdominal), fever, chills, runny nose, dry cough, nausea and vomiting, promoting loss of appetite and general malaise. Due to the large number of signs and symptoms, as well as their combinations, this health disorder is popularly called a cold and is a relatively common condition in the Brazilian population. FS usually manifests itself in mild and temporally limited signs and symptoms, usually from 5 to 7 days [1-3], but which can evolve with the inclusion of more serious symptoms such as dyspnea, respiratory distress or persistent pressure in the chest or O2 saturation less than 95% in room air or bluish color of the lips or face. thus characterizing as Severe Acute Respiratory Syndrome (SARS) [4,5].

quantitative Considering the broad and qualitative spectrum of SARS symptoms, it is estimated that more than 70% of them are associated with contamination by viral agents, such as: influenza A and B, syncytial respiratory, parainfluenza, metapneumovirus, human adenovirus, rhinovirus, enterovirus and human coronaviruses (HCoV). The common feature of these viruses is their ability to infect airway epithelial cells. From this, the host cell has its which facilitates proteins co-opted. the development of the infection. Additionally, innate and adaptive immune reactions contribute to the evolution of the symptoms that characterize the pathology. The symptomatic similarities of infection by these viral agents can lead to diagnostic limitations. However, the specific characteristics related to the conjunction of two or more highly prevalent symptoms in each viral agent, in particular, can provide important information in order to determine the suspicion about a certain causative agent [6,7].

The HCoVs were discovered in 1966, at the University of Chicago, from samples of students

with symptoms of FS. On that occasion, two types were identified and considered to cause FS. Until 2003, three more HCoVs were identified and one of them, SARS-CoV, was responsible for the SARS epidemic in 2003. This epidemic emerged in November 2002 in China, and, in just 100 days, it spread to 29 countries, infecting 8098 people and causing 774 deaths, which represents a mortality rate of 9.6%. In 2012, another type of HCoV drew attention for causing outbreaks of severe acute respiratory disease in Saudi Arabia and Jordan. Called Middle East Respiratory Syndrome (MERS), caused by MERS-CoV, the disease infected 2499 people and caused 858 deaths between 2012 and 2019 [3,8-10].

A new type of corona virus was detected in December 2019 in China, SARS-CoV-2. It is the third type of HCoV of origin that is zoonotic, as are SARS and MERS [10,11]. In early 2020, the World Health Organization (WHO) officially adopted the name COVID-19 to refer to the disease caused by the new corona virus, which is mainly due to respiratory infections ranging from mild and self-limited conditions to serious disorders, pneumonia with systemic physiological impairment. Gastrointestinal problems have been reported with increasing frequency among those diagnosed positively for COVID-19 [11,12].

The WHO classified COVID-19 as a pandemic on March 11, 2020 and nine days later the Ministry of Health of Brazil published Ordinance 454, in which the state of community transmission of the corona virus (covid-19) is declared throughout the territory national and the presence of two or more symptoms of FS is a suspected case of COVID-19, even without serological evidence or hospitalization. This is important due to the scarcity of tests to prove the SARS-CoV-2 infection and to avoid overcrowding in health facilities. Once symptoms are presented. the criteria for testing and hospitalization follow a flow that has small variations between federative units [4,5].

Based on the most recent epidemiological studies, it is possible to estimate the risk of SARS-CoV-2 infection from some symptoms that differentiate COVID-19 from other causes of FS. In this sense, the most common clinical symptoms associated with COVID-19 are fever (65% to 99%), coughing (22% to 82%), difficulty breathing (17% to 40%) in the most severe cases and muscle pain or fatigue (11% to 44%) [13-15]. In addition, loss of smell or taste was observed in about 65% of patients, being the most COVID-19. characteristic symptom of responsible for the increase of 531% to 621% in the risk of testing positive for SARS-CoV-2 [14]. Current knowledge regarding the initial symptoms of COVID-19 can help to identify about 87.5% of cases, when the loss of smell or taste is added to fever or cough [16].

Considering that Brazil is a country of continental dimensions, with great climatic and ethnic diversity plus immense social and regional inequalities, the models derived from hegemonically Asian, European and North American studies [16,15] may not accurately reflect the whole of the most prevalent and influential symptoms to predict contamination by SARS-CoV-2. Currently, both the Instituto Brasileiro de Geografia e Estatística (IBGE), which has been surveying the symptoms of FS in samples of the representative Brazilian population [17], and the Ministry of Health, responsible for coordinating disease notifications in the country, use a European model [14] to assess the probabilities contamination of the population. In addition, research on COVID-19 that incorporates the perspective of sex and race for the analysis of symptoms is scarce, although strong evidence attests that such characteristics have a significant influence on the risks of disease, death and other associated damages [18]. In this context, the objective of this study was to assess the hierarchy of symptoms characteristic of flu syndrome in patients with SARS caused by COVID-19, seen in the health system, and to develop a forecast model for potential cases of SARS-CoV-2 contamination according to sex and the race of the Brazilian population.

## 2. MATERIALS AND METHODS

This study can be characterized by its descriptive, correlational and predictive character, as well as using secondary data obtained from public access databases in Brazil, using the independent variables of sex and color

/ race of the Brazilian population as the unit of analysis. In this sense, we sought to assess the prevalence of FS symptoms associated with cases of COVID-19 in patients with SARS treated in the national health system, as well as their mortality rates. In addition to mortality, a positive diagnosis for the new coronavirus was adopted as the main outcome.

This study was developed in two stages. In the first, filtering, cleaning, reclassification and recoding of the 540,745 records available in the SARS 2020 Database (including data from COVID-19) of the Ministry of Health of Brazil [19], were carried out. So that the symptoms reported by patients seen in the health system were harmonized with those collected by National Household Sample Survey (PNAD-COVID) [17], that is, fever, cough, fatigue, nausea, headache, runny nose, dyspnea or difficulty breathing, odynophagia or pain throat, myalgia, chest pain, eve pain and loss of smell or taste. In addition to these, diarrhea and vomiting were included due to their high frequency in the participating records and their factor load in the discriminant analysis.

In filtering and cleaning the database, we sought to demarcate the records that contained the minimum information of interest, that is, date of appearance of the first symptoms, date of notification, age, sex, race, readable symptoms. diagnosis and evolution of disease. Thus, 2081 records were excluded whose date of appearance of symptoms or notification was outside the time frame of the study, that is, between February 25 and July 31, 2020, in the national health system. Another 608 records were excluded because they did not contain legible information on the symptoms presented by the patients or their gender. Records with no information on race, diagnosis and disease evolution (53,823) were kept for descriptive analysis but discarded from the hierarchical statistical modeling process.

The task of reclassification and recoding was the one that required the longest analysis time, since in the notification form of the Ministry of Health, in the symptom block there are 13 objective entries and an open or qualitative one where most of the symptoms are typed. Thus, in addition to cases of repetition of the objective entry, there were many synonyms and abbreviations that needed to be evaluated on a case-by-case basis to proceed with classification and coding according to the needs of this study. 129,539 typed symptom records were analyzed, of which 7% were duplicated and 13% illegible or incomprehensible, being excluded from the study.

In order to elaborate predictive models, the logistic regression with binary adjustment, first, the principal component analysis was reversed, on the symptoms not included in the PNAD-COVID and those whose origin was the qualitative record in the notification form, to check if there was any relevant symptom to be included in the making of the modeling. Thus, only the symptoms of diarrhea (I) and vomiting (D) were shown to be potentially relevant (Fig. 1). The choice of the number of variables to include in the predictive model was made using the lowest information criterion by Akaike [20,21].

The predictive performance of the models was measured by the Area under the Receiver Operating Characteristic Curve (AUROC) [20], which is composed of sensitivity measures (proportion of individuals who have the target condition in comparison with the positive reference standard) and specificity (proportion of individuals with a negative SARS-CoV-2 RT-PCR test and who also present negativity in the model). The general guidelines for interpreting and evaluating AUROC values (Table 1) were described by Hosmer and Lemeshow [22]. In addition, a cross-validation was performed with 30% of the eligible records, selected at random from the Ministry of Health's SARS notification database

The 405,419 records that were included in the development and testing of the forecast model were characterized by the identification of sex, race and outcome of the case. Outcome subgroups were formed to verify the differences between the prevalence of symptoms of those diagnosed as Covid-19 by the SARS-CoV-2 test by RT-PCR and those diagnosed with other pathological agents. Only records in which individuals had at least one of the seven most relevant symptoms associated with a positive diagnosis for the new corona virus were included in the final model. In addition, in the race variable, inclusion in the modeling was only for whites and blacks (blacks and browns), as the number of indigenous and yellow people was insufficient.



Fig. 1. Reverse principal component analysis (RPCA). Low prevalence symptoms are represented by letters. The lines show the Euclidean distance between the symptoms and the negative test for Covid-19 (Central point of the axes). The points represent the groups with negative diagnosis and the circle the perimeter of reliability at the level of p <0.05%

Table 1. General r	rules for interpretir	ng AUROC				
values						

Classification	AUROC
No discrimination	< 0,5
Weak discrimination	≥ 0,5 e < 0,7
Acceptable discrimination	≥ 0,7 e < 0,8
Excellent discrimination	≥ 0,7 e < 0,8
Outstanding discrimination	≥ 0,9

The basic characteristics of the subjects and symptoms are presented in the form of frequency and proportion, since they are categorical variables, and the significance of their differences was obtained by the Chi-square test, with a minimum significance of 95%. The continuous variable (age) is presented as an average and variation coefficient. All analyzes were performed using Microsoft office Excel 365 version 1708, Minitab version 3.19 and Paleontological Statistics Software Package (PAST).

## 3. RESULTS

The distribution of individuals according to sex, race and outcome (Table 2) reveals that, among those with SARS who sought assistance in health services and that there was notification, approximately 26% died from the disease. The proportion of deaths from other causes among these patients was irrelevant. However, more than 31% of cases were still ignored on the date of access to the data.

It was found that there were 48,605 more cases among men, when compared to women, and the superiority in the number of cases was independent of the subjects' race (Table 2). In this sense, men with SARS were significantly more affected by Covid-19, with a 15.5% higher risk than women. In addition, men died more than women, with a 13.8% and 15% higher risk for all causes and for Covid-19, respectively (Table 3).

The race factor also proved to be significant, with whites presenting a lower risk compared to other races in order to test positive for Sars-Cov-2. The greatest difference in risk (43.2%) occurs between whites and indigenous people, being more vulnerable to contamination by Sars-Cov-2 (Table 3). Browns were the least successful in the cure rate (40.37%) and the opposite occurred with whites, among whom, more than 49% were

cured. Among all recovered women, whose race was self-identified, white women were 36.6%. This proportion is greater than the sum of all other identified breeds (33.6%), although white is the majority. Among men, these proportions were similar, with 35.1% and 35.4% for whites and other races respectively (Table 2).

Deaths due to SARS totaled 56,997 and 76,137 people between women and men, respectively. Most of these (37.9% and 40.6%) were black women and men respectively. Deaths from other causes among SARS patients were the same (61 cases) among white and black/brown women. However, among white men, there were 41 more deaths compared to black men (Table 2). In this context, the chances of more than one non-white patient, of an identified race, affected by SARS, dying from all causes ranged from 18.4% to 38.7% and dying from Covid-19 varied from 16.7% to 64.3% (Table 3).

Those records whose race was not defined totaled 162,608 cases, that is, just over 30% (Table 2). Among these, the risk of obtaining a positive result for Sars-Cov-2 was 35.1% higher than among whites. However, the risk of death was lower, although not statistically significant (Table 3). The cure rates for this group were 29.9% for women and 29.6% for men. The death rate was 1.5% higher for women in this group compared to men (Table 2).

The evolution or result was ignored in 169,196 cases. Brown women (33.5%) and white men (36.8%) were the groups that most had their evolution, in relation to SRAG, ignored. Those who had ignored race and evolution totaled 53,823 cases, 46.6% female and 53.4% male.

Regarding the symptoms, it was found that three symptoms (fever, muscle pain and loss of smell or taste) alternate in the first three positions, in terms of Covid-19's discernment in relation to the other causes of SARS, in all stratifications performed (Fig. 2). Although dyspnea has obtained the highest prevalence (78.2% to 81.1%), this symptom has no capacity for discernment, as it is an extremely common condition in SARS due to all causes (Table 4). Loss of smell or taste, despite being the fourth least prevalent symptom (2.66% to 3.31%), received a high factor load (Fig. 2), since it is rare in patients with SARS from other causes (Table 4).

Sex	Race	Cure	Death SARS Death other		Ignored	Total	
		Freq. (%)	Freq. (%)	Freq. (%)	Freq. (%)	Freq. (%)	
Feminine	Write	40660 (36,56)	17842 (31,3)	61 (43,88)	22592 (27,46)	81155 (32,99)	
	Black	4714 (4,24)	2922 (5,13)	14 (10,07)	3559 (4,59)	11209 (4,56)	
	Yelow	999 (0,9)	612 (1,07)	00	719 (1,01)	2330 (0,95)	
	Browns	31366 (28,2)	18654 (32,73)	47 (33,81)	25453 (33,47)	75520 (30,7)	
	Indigenous	283 (0,25)	148 (0,26)	1 (0,72)	191 (0,34)	623 (0,25)	
	Ignored	33201 (29,85)	16819 (29,51)	16 (11,51)	25093 (33,03)	75129 (30,55)	
	Total	111223 (45,22)	56997 (23,17)	139 (0,06)	77607 (31,55)	245966 (100)	
Male	Write	44405 (35,06)	22860 (30,02)	108 (54,55)	26053 (36,80)	93426 (31,72)	
	Black	5695 (04,50)	3953 (05,19)	13 (06,57)	4432 (04,96)	14093 (04,78)	
	Yelow	1284 (01,01)	852 (01,12)	2 (01,01)	966 (01,14)	3104 (01,05)	
	Browns	37468 (29,58)	26927 (35,37)	54 (27,27)	31139 (34,98)	95588 (32,45)	
	Indigenous	323 (00,26)	289 (00,38)	0 (00,00)	269 (00,35)	881 (00,30)	
	Ignored	37472 (29,59)	21256 (27,92)	21 (10,61)	28730 (31,78)	87479 (29,70)	
	Total	126647 (42,99)	76137 (25,85)	198 (00,07)	91589 (31,09)	294571 (100)	
Total		237870 (44,01)	133134 (24,63)	337 (0,001)	169196 (31,30)	540537 (100)	

Table 2. Frequency and proportion of outcomes related to patients with SARS in 2020, untilJuly 31, according to sex and race

Table 3. Odds Ratio for diagnosis of Covid-19 and Death by SARS in 2020, until July 31,
according to sex and race

	Covid	-19	Death		Deaths with Covid-19		
	Odds	IC de 95%	Odds	IC de 95%	Odds	IC de 95%	
Male <sup>1</sup>	1,155	(1,1399 - 1,1695)	1,150	(1,1330; 1,1673)	1,138	(1,1165; 1,1607)	
Black	1,116	(1,0810 - 1,1514)	1,229	(1,1855; 1,2730)	1,307	(1,2467; 1,3701)	
Yelow	1,343	(1,2588 - 1,4329)	1,184	(1,1003; 1,2736)	1,167	(1,0627; 1,2813)	
Browns	1,205	(1,1860 - 1,2245)	1,191	(1,1697; 1,2136)	1,271	(1,2402; 1,3021)	
Indigenous	1,432	(1,2678 - 1,6166)	1,387	(1,2160; 1,5830)	1,643	(1,3937; 1,9376)	
Ignored	1,351	(1,3293 - 1,3731)	0,994*	(0,9752; 1,0131)	0,998*	(0,9732; 1,0226)	
_	Male <sup>1</sup> Black Yelow Browns Indigenous Ignored	Odds   Male <sup>1</sup> 1,155   Black 1,116   Yelow 1,343   Browns 1,205   Indigenous 1,432   Ignored 1,351	Odds IC de 95%   Male <sup>1</sup> 1,155 (1,1399 - 1,1695)   Black 1,116 (1,0810 - 1,1514)   Yelow 1,343 (1,2588 - 1,4329)   Browns 1,205 (1,1860 - 1,2245)   Indigenous 1,432 (1,2678 - 1,6166)   Ignored 1,351 (1,3293 - 1,3731)	Odds IC de 95% Odds   Male <sup>1</sup> 1,155 (1,1399 - 1,1695) 1,150   Black 1,116 (1,0810 - 1,1514) 1,229   Yelow 1,343 (1,2588 - 1,4329) 1,184   Browns 1,205 (1,1860 - 1,2245) 1,191   Indigenous 1,432 (1,2678 - 1,6166) 1,387   Ignored 1,351 (1,3293 - 1,3731) 0,994*	Odds IC de 95% Odds IC de 95%   Male <sup>1</sup> 1,155 (1,1399 - 1,1695) 1,150 (1,1330; 1,1673)   Black 1,116 (1,0810 - 1,1514) 1,229 (1,1855; 1,2730)   Yelow 1,343 (1,2588 - 1,4329) 1,184 (1,1003; 1,2736)   Browns 1,205 (1,1860 - 1,2245) 1,191 (1,1697; 1,2136)   Indigenous 1,432 (1,2678 - 1,6166) 1,387 (1,2160; 1,5830)   Ignored 1,351 (1,3293 - 1,3731) 0,994* (0,9752; 1,0131)	Odds IC de 95% Odds IC de 95% Odds   Male <sup>1</sup> 1,155 (1,1399 - 1,1695) 1,150 (1,1330; 1,1673) 1,138   Black 1,116 (1,0810 - 1,1514) 1,229 (1,1855; 1,2730) 1,307   Yelow 1,343 (1,2588 - 1,4329) 1,184 (1,1003; 1,2736) 1,167   Browns 1,205 (1,1860 - 1,2245) 1,191 (1,1697; 1,2136) 1,271   Indigenous 1,432 (1,2678 - 1,6166) 1,387 (1,2160; 1,5830) 1,643   Ignored 1,351 (1,3293 - 1,3731) 0,994* (0,9752; 1,0131) 0,998*	

<sup>1</sup> In relation to the female sex; <sup>2</sup> Regarding the white race; \* Not significant (p> 0.05)

Another five symptoms were relevant for signaling covid-19 infection in the Brazilian population, namely: headache, fatigue, vomiting, diarrhea and cough (Fig. 2). However, some of them are specific to certain groups. Coughing (67.7% to 75.1%), for example, was relevant for white male subjects. However, among white women, the symptom was not relevant, as well as for the other groups (Table 4). Another symptom that seems to be more related to a specific group was odynophagia but known as sore throat (19.5% to 22.6%), which was relevant only for black men (Fig. 2). Altogether, the sum of the six or seven most relevant symptoms for each group predicts 63% of possibility of infection by covid-19 the (Fig. 3B) and increases the chance of testing positive for this disease by 221% when compared with patients without such symptoms (Fig. 3A).

#### 4. DISCUSSION

The number of hospitalizations due to SARS in Brazil, in 2020, since the first case of Covid-19 was registered, greatly exceeded the upper limit of the confidence interval of the trend curve of the last ten years [23]. For Bastos et al. [12], the SARS surveillance system in Brazil presents problems in registering information on notifications and lack of tests for the new corona virus, which can lead to underreporting of cases and deaths by Sars-Cov-2. This is reflected in the data in Table 2, where those whose race and evolution were ignored totaled 53,823 cases, 46.6% female and 53.4% male. These cases were excluded from the modeling of this study for obvious reasons, but they should be considered in order to make health professionals aware of the importance of the correct registration and notification of cases, even under the abnormal pressure caused by the new coronavirus.

The creation of strategies for screening and monitoring people with suspicious signs and symptoms, or confirmed with Covid-19, through different tools such as virtual applications, telephone calls, screening in health services and public agents acting in the territory in order to understand the symptomology of the disease with updated data on the course of the disease are extremely important actions for countries where social and economic inequality is excessive. However, without good administrative records, these tasks become more difficult and expensive [14,24,25]. Brazil is a country widely recognized for the immense differences in living conditions of the various groups of its population. The secular heritage of slavery, based on racial criteria, is associated with the fact that the majority of the black population is poor or in extreme poverty [26,27]. This condition is related to difficulties in accessing the health system, predominance of on-the-job work and income activities, houses with few rooms that hinder home isolation and especially in the urban environment. neighborhoods with territories with greater demographic density [17].



Fig. 2. Hierarchical symptoms presented by patients with SARS caused by SARS-COV-2, until July 31, according to sex and race. Just statistically relevant symptom in the hierarchy



Fig. 3. Conjugated and hierarchical odds ratio, according to the number of symptoms, adjusted for sex and race, compared with a random control group of 30% of patients to test the effect of sample size (A). Equation, ROC and AUROC curve of the forecasting model (B), where, age (years), symptom (present = 1, absent = 0), sex (feminine = 1, masculine = 0) and race (black = 1, white = 0)

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Symptoms	Feminine (%)				Male (%)			
	White		Black		White		Black	
	Covid-19	Other	Covid-19	Other	Covid-19	Other	Covid-19	Other
Loss of smell / taste	3,27	0,85	3,31	1,23	2,67	0,78	2,66	1,11
Headache	9,83	6,06	9,9	6,64	7,93	4,6	7,89	4,82
Runny nose	26,6	26,7	25,2	27,8	24,1	24,9	21,7	25,4
Diarrhea	16,4	12,54	14,48	12,41	14,1	10,99	12,86	10,8
Dyspnea	78,2	81,08	78,17	80,11	78,97	80,39	80,16	81,03
Chest pain	0,46	0,5	0,54	0,55	0,49	0,53	0,48	0,56
Eye Pain	0,07	0,02	0,08	0,02	0,07	0,02	0,07	0,02
Fatigue	3,83	2,07	3,67	2,34	3,8	2,07	3,53	2,43
Fever	62,1	55	65,55	59,38	69,85	59,42	71,89	63,02
Myalgia	10,4	5,58	9,08	5,57	10,71	5,1	8,73	5,16
Nausea	1,74	1,19	1,24	0,98	1,27	0,9	0,89	0,64
Odynophagia	21	19,63	22,6	20,87	19,46	16,73	21,8	18,51
Other Symptom	46,6	36,66	45,17	37,82	44,05	34,86	41,72	35,37
Cough	72,7	67,72	72,85	69,81	74,93	69,51	75,08	71,44
Vomiting	10,1	11,18	12,1	9,59	7,33	9,73	7,05	9,5

Table 4. Symptoms presented by patients with SARS, according to sex and race, caused by SARS-COV-2 and other pathological agents<sup>1</sup>

<sup>1</sup> Cells of the same color indicate statistically significant differences (p < 0.05) between Covid-19 and other pathological agents that cause SARS, according to the chi-square

test

The limitations and living conditions imposed by race-related poverty can affect the prevalence and evolution of symptoms of contagious diseases like Covid-19 [28,29]. Our study showed that the proportion of cured people was lower among blacks compared to whites and that of deaths was higher (Table 2). Thus, the chances of a black man dying from SARS caused by Sars-Cov-2 was almost 30% higher. Additionally, the situation of the indigenous group was even worse, with a 64.3% higher chance compared to whites (Table 3).

There is almost universal consensus among health professionals that the primary symptoms, which serve as indicators for infection caused by the new corona virus, are respiratory problems and fever [16,30]. However, as the pandemic persists and advances internationally, new records indicate a wide variety of symptoms unknown until then [9]. Over time, the new virus has spread to different regions and has reached people of all ethnicities, styles and living conditions. As a result, different signs and symptoms appeared, such as loss of smell and taste, fatigue, muscle or joint pain, headache, weakness, nausea, diarrhea, dizziness, tremor, chills, hyporexia, hair loss and skin rashes, including in the mouth [11,31,32].

As Brazil is a country of continental scale, which presents great environmental, cultural and ethnic-racial diversity, in addition to immense inequality of living conditions in its population [24], the set of symptoms in response to infection by Covid-19 also presents great variability (Fig. 2) and makes it difficult to predict positive cases based on symptoms, even in patients with SARS [14,17]. According to GENDRO [18]. the evidence that the incidence, prevalence and mortality of Covid-19, as well as its determinants and socioeconomic impacts are strongly influenced by gender and race inequalities. In this sense, Fig. 2 demonstrated that, although the three most relevant symptoms are common to all groups, symptoms considered relevant in other studies [11,12,16,13,31,33], such as cough, may be related specific sex and race (white men). On the other hand, odynophagia seems to be a relevant symptom only for black men (Table 4).

A fact that draws attention in our study is the difference in the prevalence of symptoms of loss of smell or taste in Brazilian patients (Table 4) compared to European and North American patients (about 65%) [14]. Recent data from the

National Household Sample Survey (PNAD-COVID) confirm the low prevalence of this symptom in the Brazilian population [17]. Studies in countries with a non-white population majority report results like those presented in Table 4 [34,35]. This wide range of prevalence related to the loss of smell or taste may be due to differences in methods and periods where data were collected. In addition to great differences in the intensities of socioeconomic inequalities and climatic variability, as well as, in the level of racial diversity and miscegenation.

In Brazil, mass testing is not yet an action adopted in all states. Therefore, until the end of July 2020, there was still no information on contagion on a population scale. Studies carried out with populations in Europe, USA and Israel made well-adjusted models to estimate the risk of infection by Covid-19 [16-14,25]. Although these studies are subject to bias, since the samples are not random, they obtained AUROC above 70%, which was not the case (Fig. 3B). Probably, the difficulty in modeling the risk of Sars-cov-2 infection for the Brazilian population based on symptoms reported in PNAD-COVID, is related to the selection bias of the eligible records of the FS and SARS surveillance system, in addition to the greater environmental, racial and socioeconomic diversity and inequality of the Brazilian population in relation to the countries that have been successful in this type of modeling [28-37].

## **5. CONCLUSION**

Therefore, it is concluded that the factors sex and race, characterized by great diversity and inequality in Brazil, can influence the hierarchy and variability of the symptoms of infection with the new corona virus in patients with SARS. As a result, the development of a statistical model to predict the probability of positive cases based on symptoms reported by the population can be a more complicated challenge than in other countries. This finding highlights the urgency of the need to expand population surveys such as PNAD-COVID, including information on individual testing in probabilistic and representative samples of the main ethnic-racial, socioeconomic and territorial strata, in order to produce models capable of estimating specific probabilities of contamination by this pathological agent and provide decision makers with relevant and clear information to help them allocate scarce public resources more precisely, especially those destined for mass testing and preventive expansion of the number of beds available to treat victims of covid-19.

## CONCENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

## ETHICAL APPROVAL

This study does not contain any studies with human participants or animals performed by any of the authors.

## **COMPETING INTERESTS**

Authors have declared that no competing interests exist.

## REFERENCES

- Alfradique ME, Bonolo PF, Dourado I, Lima-Costa MF, Macinko J, Mendonça CS, Oliveira VB, Sampaio LFR, Simoni C, Turci MA. Hospitalizations for conditions sensitive to primary care: The construction of the Brazilian list as a tool to measure the performance of the health system (Project ICSAP - Brazil). Reports in Public Health. 2009;25(6):1337-1349.
- Cardoso CS, Pádua CM, Rodrigues-Júnior AA, Guimarães DA, Carvalho SF, Valentin RF, Abrantes R, Oliveira CDL. Contribution of hospitalizations for primary caresensitive conditions to the profile of admissions in the public health care system. Pan American Journal of Public Health. 2013;34(4):227-234.
- Stellrecht KA. Molecular testing for respiratory viruses. In: Coleman WB, Tsongalis GJ, editors. Diagnostic molecular pathology: A guide to applied molecular testing. Academic Press. 2016;123-137.
- Ministry of health (Brazil). Ordinance n° 454, of March 20, 2020. It declares, throughout the national territory, the state of community transmission of the coronavirus (COVID-19); 2020. Accessed 07 September 2020. Available:https://www.in.gov.br/en/web/dou /-/portaria-n-454-de-20-de-marco-de-2020-249091587
- 5. State department of health (Paraíba, Brazil). Protocols: State center for the dissemination of health evidence from

COVID-19 of the Paraíba state health secretariat (CDES-COVID19); 2020. Accessed 07 September 2020. Available:https://paraiba.pb.gov.br/diretas/s aude/coronavirus/evidenciascientificas/arquivos/criterios-parainternacao-hospitalar-em-enfermaria-ouuti-no-cenario.pdf

- Dong J, Ismail N, Walker DH. Molecular testing in emerging infectious diseases. In: Coleman WB, Tsongalis GJ, editors. Diagnostic molecular pathology: A guide to applied molecular testing. Academic Press. 2016;179-200.
- Nedel FB, Facchini LA, Martín M, Navarro A. Primary health care risk factors for hospitalization for ambulatory care sensitive conditions: Systematic literature review. Epidemiology and Health Services. 2010;19(1):61-75.
- Hamre D, Procknow JJ. A new virus isolated from the human respiratory tract. Proc Soc Exp Biol Med. 1966;121(1):190-193.
- 9. Oliveira FMS. Human coronavirus detection in pediatric patients with pneumonia treated at a reference hospital in Fortaleza-CE in the years 2011 and 2012; 2014.

Accessed 07 September 2020. Available:http://www.repositorio.ufc.br/han dle/riufc/15383

- 10. Memish ZA, Perlman S, Kerkhove MDV, Zumla A. Middle East respiratory syndrome. Lancet. 2020;395(10229):1063-1077.
- Gulati A, Pomeranz C, Qamar Z, Thomas S, Frisch D, George G, Summer R, DeSimone J, Sundaram B. A comprehensive review of manifestations of novel coronaviruses in the context of deadly COVID-19 global pandemic. The American Journal of the Medical Sciences. 2020;360(1):5-34.
- Bastos LS, Niquini RP, Lana RM, Villela DAM, Cruz OG, Coelho FC, Codeço CT, Gomes MFC. COVID-19 and hospitalizations for SARS in Brazil: A comparison until the 12th epidemiological week of 2020. Reports in Public Health. 2020;36(4):e00070120.
- Sun L, Song F, Shi N, Liu F, Li S, Li P, Zhang W, Jiang X, Zhang Y, Sun L, Chen X, Shi Y. Combination of four clinical indicators predicts the severe/critical symptom of patients infected COVID-19.

Journal of Clinical Virology. 2020;128: 104431.

- Menni C, Valdes AM, Freidin MB, Sudre CH, Nguyen LH, Drew DA, Ganesh S, Varsavsky T, Cardoso MJ, Moustafa JSE, Visconti A, Bowyer PHRCE, Mangino M, Falchi M, Wolf J, Ourselin S, Chan AT, Steves CJ, Spector TD. Real-time tracking of self-reported symptoms to predict potential COVID-19. Nature Medicine. 2020;26(7):1037-1040.
- Liu J, Xie W, Wang Y, Xiong Y, Chen S, Han J, Wu Q. A comparative overview of COVID-19, MERS and SARS: Review article. International Journal of Surgery. 2020;81:1-8.
- Menni C, Sudre CH, Steves CJ, Ourselin S, Spector TD. Quantifying additional COVID-19 symptoms will save lives. Lancet. 2020;395(10241):107-108.
- 17. Brazilian institute of geography and statistics. Continuous national household sample survey (PNAD) COVID-19; 2020. Accessed 07 September 2020. Available:https://www.ibge.gov.br/estatistic as/sociais/trabalho/27946-divulgacaosemanal-

pnadcovid1.html?=&t=microdados

 Advancing sex and gender equity in research – GENDRO. A call for urgent action: A renewed commitment to gender responsive research for health equity and human rights in the context of COVID-19 Pandemic; 2019.

Accessed 07 September 2020.

Available:https://www.gendro.org/statemen ts

 Ministry of health (Brazil). SRAG 2020 -Severe Acute Respiratory Syndrome Database - including data from COVID-19; 2020.

Accessed 07 September 2020.

Available:https://opendatasus.saude.gov.br /dataset/bd-srag-2020

- 20. Byrne S. A note on the use of empirical AUC for evaluating probabilistic forecasts. Electronic Journal of Statistics. 2016;10(1): 380-393.
- 21. LeDell E, Petersen M, Laan MVD. Computationally efficient confidence intervals for cross-validated area under the ROC curve estimates. Electronic Journal of Statistics. 2015;9(1):1583-1607.
- 22. Hosmer D, Lemeshow S. Applied logistic regression. 3rd ed. Hoboken, New Jersey: John Wiley & Sons Inc; 2013.

23. Cota W. Monitoring the number of COVID-19 cases and deaths in Brazil at municipal and federative units level. SciELO Preprint; 2020.

Accessed 07 September 2020. Available:https://preprints.scielo.org/index. php/scielo/preprint/view/362

24. Pires LN, Carvalho L, Xavier LL. COVID-19 and inequality: The distribution of risk factors in Brazil. Experimental Findings; 2020.

Accessed 07 September 2020. Available:https://www.researchgate.net/pu blication/340452851\_COVID-19 e Desigualdade no Brasil

- Rossman H, Keshet A, Shilo S, Gavrieli A, Bauman T, Cohen O, Shelly E, Balicer R, Geiger B, Dor Y, Segal E. A framework for identifying regional outbreak and spread of COVID-19 from one-minute populationwide surveys. Nature Medicine. 2020; 26(5):634-638.
- Calmon TVL. Objective conditions for confronting COVID 19: Brazilian social abyss, racism, and social development perspectives as determinants. NAU social magazine. 2020;11(20):131–136.
- 27. Brazilian Institute of geography and statistics. Social inequalities by color or race in Brazil. Rio de Janeiro: IBGE; 2019.
- Dye TDV, Muir E, Farovitch L, Siddiqi S, Sharma S. Critical medical ecology and SARS-COV-2 in the urban environment: A pragmatic, dynamic approach to explaining and planning for research and practice. Infect Dis Poverty. 2020;9(1):71-78.
- 29. Victora CG. Socioeconomic inequalities in Health: Reflections on the academic production from Brazil. International journal for equity in health. 2016;15(1):164-167.
- zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, Xiang J, Wang Y, Song B, Gu X, Guan L, Wei Y, Li H, Wu X, Xu J, Tu S, Zhang Y, Chen H, Cao B. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: A retrospective cohort study. Lancet. 2020; 395(10229):1054-1062.
- Jiang F, Deng L, Zhang L, Cai Y, Cheung CW, Xia Z. Review of the clinical characteristics of coronavirus disease 2019 (COVID-19). Journal of general internal medicine. 2020;35(9):1545–1549.
- 32. Ministry of health (Brazil). Coronavirus; 2020.

Accessed 07 September 2020.

Available:https://coronavirus.saude.gov.br/ sobre-a-doenca

- Spinato G, Fabbris C, Polesel J, Cazzador D, Borsetto D, Hopkins C, Boscolo-Rizzo P. Alterations in smell or taste in mildly symptomatic outpatients with SARS-CoV-2 infection. JAMA. 2020;323(20):2089-90.
- 34. Bagheri SHR, Asghari AM, Farhadi M, Shamshiri AR, Kabir A, Kamrava SK. Coincidence of COVID-19 epidemic and olfactory dysfunction outbreak. medRxiv; 2020.

Available:http://dx.doi.org/10.1101/2020.03 .23.20041889

- Mao L, Wang M, Chen S, He Q, Chang J, Hong Cc. Neurological manifestations of hospitalized patients with COVID-19 in Wuhan, China: A retrospective case series study. JAMA Neurol. 2020;77:683-90.
- Eslami H, Jalili M. The role of environmental factors to transmission of SARS-CoV-2 (COVID-19). AMB Expr. 2020;10(1):92.
- Penna GO, Silva JAA, Neto CJ, Temporão JG, Pinto LF. PNAD COVID-19: A powerful new tool for public health surveillance in Brazil. Collective science and health. 2020; 25(9):3567-3571.

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