Clinical characteristics of Severe Acute Respiratory Syndrome by COVID-19 in Indigenous of Brazil

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Abstract

Background: The indigenous people of Brazil present several cases and deaths, affecting 158 peoples, with high vulnerability and limited access to health services. **Objective:** Investigate the clinical characteristics of severe acute respiratory syndrome by COVID-19 in indigenous peoples of Brazil. **Method:** The epidemiological, cross-sectional, and analytical study, from the data of the platform opendataSUS referring to the SIVEP-GRIPE in the period of 01/01/2020 until 31/08/2020. Profile variables, signs and symptoms, and risk factors/comorbidities. The data were analyzed by Bioestat 5.3. **Results:** 1,207 cases and 470 deaths. Profile: male gender (59.48%) mean age 53. Signs and symptoms: fever (74.23%), cough (77.71%), sore throat (35.62%), dyspnea (69.34%), respiratory discomfort (62.80%), O2 saturation <95% (56.42%); and associated with mortality: dyspnea (80.0%) and O2 saturation <95% (69.36%). Risk factors and comorbidities (45.89%) were associated with deaths (54.04%). Comorbidities: Chronic Cardiovascular Disease (18.97%) and Diabetes Mellitus (18.97%), and associated with deaths: Chronic Cardiovascular Disease (24.46%). There was significance in the survivors vaccinated for influenza (26.18%). **Conclusion:** The public and health policies of Brazil should be directed to control the dissemination of COVID-19 in this population, that COVID-19 evolves in the same intensity, however, the indigenous have vulnerabilities that can enhance the impact of the pandemic in this population.

Key-words: Severe Acute Respiratory Syndrome; Indigenous People; SARS-CoV-2; COVID-19; Brazil.

INTRODUCTION

Severe Acute Respiratory Syndrome (SARS) is a severe respiratory illness characterized by the presence of flu symptoms associated with dyspnea or respiratory discomfort or persistent pressure in the chest or oxygen saturation (O2) <95% or facial cyanosis[1]. It is caused by several etiologies such as (influenza A, dengue, respiratory syncytial virus, adenovirus, hantavirus, and coronavirus), and other agents (pneumococci, other bacteria, *Legionella* sp., leptospirosis, etc.)[2].

Regarding viral etiologies, they are capable of causing major epidemics in the world, such as those caused by two coronaviruses, SARS-CoV characterized in 2003 by SARS in China, which spread to 29 countries and regions, and MERS-CoV (Middle East Respiratory Syndrome) in 2012 in Saudi Arabia. The transmission of both was through respiratory droplets directly and indirectly and most of the cases proved to be mild[3].

Coronaviruses are single tape RNA viruses with envelope. The glycoprotein (S) peaks around the spherical verion give the virus its characteristic "halo appearance", i.e., a crown in electron microscopy. Six subgroups of coronavirus are human pathogens, the subgroup α coronavirus includes 229E and NL229E and the subgroup β coronavirus includes OC43, HKU1, SARS-CoV, and MERS-CoV[4]. The pathophysiological mechanism in SARS-CoV and MERS-CoV is performed by binding in the angiotensin-converting enzyme 2 (ACE2) and is expressed in many human organ tissues, being highly expressed in the lungs, heart, and small intestine, however, the presence of ACE2 may not be the only requirement for tropism[5,6].

In December 2019, cases of severe pneumonia of unknown etiology appeared in Wuhan, China, with the association of the cases to a market in the region. In January 2020 the infectious agent was isolated, being of the type coronavirus. Thus it was named SARS-CoV-2 for its similarity to SARS-CoV and the disease named COVID-19, also presenting several other similarities such as the pathophysiological and transmissibility mechanism[7]. In March 2020 the World Health Organization (WHO) declared the outbreak of SARS-CoV-2 as a pandemic, the first case confirmed in Brazil in February 2020[8,9].

The literature cites risk factors for severity at COVID-19 such as chronic disease carriers, the elderly, obese and pregnant women, generally severe cases require intensive care and longer hospital stay and high mortality[10,11]. However, studies do not show the impact and characteristics of COVID-19 on the indigenous population.

The epidemiological surveillance of COVID-19 in Brazil is performed from two online platforms: E-SUS notifies and SIVEP-GRIPE. E-SUS notifies is an exclusive platform for

suspected and confirmed cases of influenza syndrome (IS) by COVID-19 and SIVEP-GRIPE is a platform that performs surveillance of SARS by all etiologies, among them COVID-19, so SIVEP-GRIPE notifies any case of hospitalized SARS or death by SARS regardless of hospitalization[1].

In Brazil, according to COVID-19's monitoring platform on Indigenous Peoples, based on data from the Articulation of Indigenous Peoples of Brazil (APIB), it shows that on 20/09/2020 it already had 32,615 cases on Indigenous Peoples, 818 deaths, and 158 affected peoples[12]. Another agency that performs surveillance of cases in indigenous people in Brazil is the Special Secretariat of Indigenous Health (SESAI), which reported the occurrence of 26,723 cases and 426 deaths, with a mortality rate of 1.59%.[13]. The difference in information is observed, in the deaths is double, this shows the underreporting of cases in this population, as well as the ignorance of this disease in this group.

It stands out for the indigenous peoples, their characteristics with the worst human development rates. They have precarious and limited access to health services, high infant mortality rates, and the main diseases that affect them are tuberculosis, verminous, diarrhea, and respiratory infections. It is also worth mentioning that institutional racism and the continuous loss of their land also result in food quality and lack of assistance. Because of the preservation of biodiversity and culture, these people live in rural and distant places, which increases vulnerability, where public policies do not yet reach associated with extreme poverty[14].

Due to the vulnerability of indigenous peoples and the difference in information between APIB and SESAI, and the importance of knowing the clinical characteristics and factors associated with mortality, which becomes crucial for the development of intervention and prevention strategies. In this perspective, this study aims to investigate the clinical characteristics of severe acute respiratory syndrome by COVID-19 in indigenous Brazil.

METHOD

The cross-sectional and analytical epidemiological study, quantitative, of secondary base data, from data made available by the openDataSUS platform (https://opendatasus.saude.gov.br/) of the Ministry of Health of Brazil [15], regarding the surveillance data of Severe Acute Respiratory Syndromes (SARS), from the platform of Information System for Epidemiological Surveillance of Influenza (SIVEP-GRIPE) corresponding to the period from 01/01/2020 until 31/08/2020 of the notifications. (https://sivepgripe.saude.gov.br/sivepgripe/login.html?1).

The bank was obtained from the OpenDataSUS platform in Excel 2019 format, on the date of 09/05/2020, with the last update on 08-31/2020, the bank refers to SARS cases from 01/01/2020 to 08-31/2020. The SIVEP-GRIPE notification form is composed of 80 variables, referring to socio-demographic and clinical-epidemiological data (https://opendatasus.saude.gov.br/dataset/ae90fa8f3e94467ea33f94adbb66edf8/resource/54a46c6d-e0b5-40b7-8b74-85450d22ace3/download/ficha-srag-final-27.07.2020_final.pdf). The variables extracted according to the form were: sex (item 8), age (item 10), signs and symptoms (item 35), has risk/comorbidities factors (item 36), took flu vaccine (item 37), final classification: 5-SARS by COVID-19 (item 72) and evolution:2- death (item 74).

The inclusion criteria were notifications of residents in Brazil, the indigenous race, and final SARS classification by COVID-19. Blank notifications were excluded.

The data were organized in an Excel 2019 spreadsheet, and the analysis was performed by the *Bioestat 5.3* statistics program. We used the chi-square statistical tests of adherence for equal expected proportions, chi-square: independence test, and test G (Table of Contingency L x C) in equal or <5 values, to associate the significant variables in the 95% confidence interval between survivors and deaths. The results were presented in tables.

The data of this study were made publicly available, not containing personal data of patients such as name, address, and telephone contact, thus not presenting risks to the participants of the research, as well as being dispensed with the ethical opinion. This study is by Law No. 12,527 of 18/11/2011 (Law of Access to Information) [16].

RESULTS

The database (DB) shows a total of 670,929 notifications, including negative ones, awaiting results and confirmed ones: (1) SARS due to influenza, (2) SARS due to another respiratory virus, (3) SARS due to another etiologic agent, (4) SARS unspecified and (5) SARS due to COVID-19. Thus, the indigenous race was filtered in the DB which resulted in 1,991 notifications with those confirmed for COVID-19, resulting in 1,207 notifications.

Table 1 shows the profile of the indigenous people about sex and age group, being most of the cases male (718; 59.48% $p<0.0001$), predominating also the male sex in the deaths (314; 66.80% $p<0.0001$). About the age group, the average of the cases was 53 years, over the survivors the majority was between 21 and 50 years; already about the deaths, it was distinguished the >60 years (309; 65.74% $p<0.0001$) with the average of 64 years. Between 0

and 20 years there was no statistical difference between survivors and deaths, as well as between 51 and 60 years.

Table - 1 - Profile of Severe Acute Respiratory Syndrome by COVID-19 in Indigenous Brazil, 2020.

Profile	**Total (1.207:%)**	**Survivors (737:%)**	**Deaths (470:%)**	**X^2**	**P-valor****	**P-Value *****
Sex						
Female	489:40,51	**333:45,18**	156:33,19	16,630		
Male	**718:59,48**	404:54,81	**314:66,80**	16,630	< 0,0001	
Expected proportions equal	< 0,0001*	0,0099*	< 0,0001*			
Age						
Minimum - Maximum	0 -110	0 - 107	0 - 110			
Average	53	48	64			
0 to 10	104:8,61	77:10,44	27:5,74	7,475		
11 to 20	31:2,56	27:3,66	4:0,85	9,1564		0,1906
21 to 30	74:6,13	**66:8,95**	8:1,70	24,998		0,0849
31 to 40	92:7,62	**74:10,04**	18:3,82	14,853	< 0,0001	0,8821
41 to 50	166:13,75	**131:17,77**	35:7,44	24,944		0,6487
51 to 60	190:15,74	121:16,41	69:14,68	0,528		< 0,0001
> 61	550:45,56	241:32,70	**309:65,74**	125,012		< 0,0001

Source: SIVEP-GRIPE, OpendataSUS, Ministry of Health 2020. * Chi-square grip. ** Chi-square independence. chi-square partition.

The clinical characteristics (Table 2) regarding the most evident signs and symptoms were: Fever (896:74.23%), Cough (938:77.71%,) Sore throat (430:35.62%), Dyspnea (837:69.34%), Respiratory Discomfort (758:62.80%), O2 Saturation <95% (681:56.42%). The signs and symptoms associated with mortality were dyspnea (376:80.0% p<0.0001) and O2 saturation <95% (326:69.36%) p<0.0001). The presence of risk factors and comorbidities (554:45.89%) was also associated with deaths (253:54.04% p<0.0001). The most evident comorbidities were: Chronic Cardiovascular Disease (229:18.97%) and Diabetes Mellitus (229:18.97%). The only comorbidity associated with deaths was Chronic Cardiovascular Disease (115:24.46% p<0.0002). Those vaccinated for influenza showed significance in survivors (193:26.18% p<0.0001).

Table - 2 - Clinical Characteristics of Severe Acute Respiratory Syndrome by COVID-19 in Indigenous Brazil, 2020.

Clinical Characteristics	Total (1.207:%)	Survivors (737:%)	Deaths (470:%)	X^2	P-value (survivors vs. deaths)
Fever	896:74,23	551:74,76	345:73,40	0,210	0,6465
Cough	938:77,71	568:77,06	370:78,72	0,363	0,5469
Sore Throat	430:35,62	262:35,54	168:35,74	0,000	0,9941
Dyspnea	837:69,34	461:62,55	**376:80,0**	40,288	< 0,0001
Respiratory discomfort	758:62,80	435:59,02	323:68,72	11,148	0,0008
O2 saturation <95%	681:56,42	355:48,16	**326:69,36**	51,567	< 0,0001
Diarrhea	177:14,66	108:14,65	69:14,68	0,005	0,9437
Vomit	117:9,69	74:10,04	43:9,14	0,169	0,6812
Altered chest X-ray	441:36,53	266:36,09	175:37,23	0,116	0,7336
Other	338:28,00	220:29,85	118:25,10	2,973	0,0847
Risk Factors and Comorbidities	554:45,89	301:40,84	**253:54,04**	18,978	< 0,0001
Pregnant	35:2,89	**35:4,74**	0:0,00	30,3464	< 0,0001
Puerpera	11:0,91	10:1,35	1:0,21	3,4667	0,0626
Chronic Cardiovascular Disease	229:18,97	114:15,46	**115:24,46**	14,541	< 0,0002
Chronic Hematological Disease	8:0,66	4:0,54	4:0,85	0,0774	0,7809
Down syndrome	4:0,33	0:0,00	4:0,85	4,0945	0,0430
Chronic Liver Disease	9:0,74	2:0,27	7:1,48	4,1240	0,0423
Asthma	23:1,90	13:1,76	10:2,12	0,055	0,8143
Diabetes Mellitus	229:18,97	120:16,28	109:23,19	8,468	0,0036
Chronic Neurological Disease	14:1,15	5:0,67	9:1,91	2,7326	0,0983
Another Chronic Pneumopathy	24:1,98	10:1,35	14:2,97	3,086	0,0790
Immunodepression	18:1,49	7:0,94	11:2,34	2,891	0,0891
Chronic Kidney Disease	41:3,39	16:2,17	25:5,31	7,735	0,0054
Obesity	27:2,23	15:2,03	12:2,55	0,155	0,6938
Other	199:16,48	113:15,33	86:18,29	1,624	0,2026
Influenza vaccination	264:21,87	**193:26,18**	71:15,10	19,977	< 0,0001

Source: SIVEP-GRIPE, OpendataSUS, Ministry of Health 2020.

DISCUSSION

This study highlighted the clinical characteristics of SARS in indigenous Brazilians with an average age of 53 years (59.48%), being similar to a study [17] in non-indigenous patients hospitalized for SARS/COVID-19, however, the average age was 62 years, but approaching the results of two other studies with patients hospitalized for SARS by COVID-19 in non-indigenous patients, in one the average was 55 years, and in the other 50 years [18,19]. Therefore, there are no discrepancies between the average age and sex, between indigenous and non-indigenous people in SARS by COVID-19.

Concerning sex, it was significant in the deaths of the male (66.80%) with a mean age of 64 years. A large study with 17,278,392 cases, and concerning the deaths that were 10,926, identified the male gender and higher age as a predictor for mortality by COVID-19[20]. Another survey compared the deaths by COVID-19 from Italy 1,625 and China 1,023, and both were significant in individuals over 70 years, however, the lethality in Italy was higher (7.2%) because the infected were older, already in China was (2.3%)[21]. In these studies, cited were not specifically with indigenous people, but it is observed the similarity in the variables associated with death by COVID-19.

The most evident signs and symptoms in this study were fever (74.23%), cough (77.71%,) sore throat 35.62%), dyspnea (69.34%), respiratory discomfort (62.80%), O2 saturation <95% (56.42%). These results were similar in several studies[22–25], showing the classical picture of SARS associated with pulmonary involvement, evidenced by imaging examination, such as chest tomography [26]. This was also evident in this study the radiographic alterations in 36.53% of the cases. The Brazilian Ministry of Health established criteria for the definition of clinical diagnosis-imaging, in the impossibility of performing the molecular test or epidemiological link, and thus associated with the clinical characteristics the tomography should evidence by one of these changes: opaqueness in bilateral, peripheral frosted glass, with or without consolidation or visible intralobular lines ("paving"), or opaqueness in the multifocal frosted glass of rounded morphology with or without consolidation or visible intralobular lines ("paving"), or sign of reverse halo or other findings of pneumonia in an organization (observed later in the disease)[1].

Regarding deaths, the associated signs and symptoms were dyspnea (80.0%) and O2 saturation <95% (69.36%). Dyspnea and O2 saturation less than 95% indicate severe pulmonary involvement, which requires intensive care and mechanical ventilation if O2

saturation does not reach up to 92% with noninvasive oxygen therapy[27]. Studies relate the pulmonary involvement of other organs such as the heart to a storm of inflammatory cytokines, characterized by a sudden acute increase in circulating levels of different pro-inflammatory cytokines, IL-6, IL-1, TNF-α, and interferon, caused by the activation of several immune cells such as macrophages, neutrophils and T cells from the circulation to the site of infection causing damage to the vascular barrier, capillary damage, diffuse alveolar damage and multi-organ failure[28–30]. Thus, hyper inflammation influences O2 saturation drop and myocardial stability complications, causing the cardiopulmonary deficiency, with acute cardiac injury and lung injuries, which are serious complications directly associated with mortality[31,32].

The presence of risk factors and comorbidities (45.89%) of the cases was also evidenced, as well as associated with the deaths (54.04%). The most prevalent comorbidities were chronic heart diseases (18.97%) and diabetes (18.97%). However, the only significant comorbidities separately associated with deaths were chronic heart diseases (24.46%). Being corroborated by several types of research [33–35], However, the studies also showed not only heart disease as a factor of complications and deaths but also diabetes, obesity, and chronic lung disease, specifically the most significant comorbidity in these studies was hypertension and diabetes. A meta-analysis with 1,527 cases, showed that the prevalence of hypertension, diabetes, and cerebrovascular diseases, were evident two to three times more in patients hospitalized by COVID-19 in the Intensive Care Unit, than those who were in the ward, as they also highlighted the systemic complications, the most evident being the acute cardiac injury in 8%, directly associated to mortality[36]. In this way, the results meet the literature.

For the variable "to be vaccinated against the flu" there was significance in the survivors (26.18%). A research in Italy over 65 years old with high vaccination coverage of influenza, detected the association with a reduced spread and a less severe clinical expression of COVID-19[37]. A study highlights that mass immunization against influenza in the COVID-19 pandemic aims to minimize cases of co-infection that can be a factor of severity and mortality, as well as protecting risk groups that are similar in both diseases[38]. Thus, a similar result is shown in those vaccinated against influenza as a protection factor for severity of COVID-19, however, no studies are explaining this mechanism.

The limitation of this research is that there are no studies of SARS by COVID-19 in the indigenous population, and it is not possible to compare the variables, however, it was possible to compare the clinical characteristics with other ethnic groups or even general. As well, it was shown the similarity in the different population groups, showing that COVID-19 presents in the same intensity and needs attention in these groups as indigenous since these people have

limited access to health services, as well as the prevalence of other diseases that can potentialize the complications of COVID-19.

CONCLUSION

It was possible to evidence the clinical characteristics of Severe Acute Respiratory Syndrome in Indigenous Brazil, from the data of SIVEP-GRIPE. They are mostly male, both in cases and deaths, in cases of adults and older deaths, the most common signs and symptoms being fever, cough, sore throat, dyspnea, respiratory discomfort, and O2 saturation <95%, however, the signs and symptoms associated with the deaths were dyspnea and O2 saturation <95%. The most prevalent comorbidities were chronic heart disease which was associated with deaths and diabetes.

Another relevant finding was that those vaccinated against influenza died less than those not vaccinated, showing a possible relation of protection in influenza vaccine, however, there is no scientific explanation so far.

It is emphasized that Brazil's public and health policies are directed towards controlling the spread of COVID-19 in the indigenous populations since it has been shown that the disease evolves in the same intensity in this group, however, the indigenous have vulnerabilities that can potentialize the impact of this pandemic on this population.

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