Clinical characteristics and outcomes of Brazilian patients with severe acute respiratory syndrome coronavirus 2 infection: an observational retrospective study

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ORIGINAL ARTICLE

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ABSTRACT

BACKGROUND: Since February 2020, data regarding clinical features and patients' clinical evolution of Brazilian patients have been required to understand the development of the disease in the country.

OBJECTIVE: To assess clinical features of Brazilian patients infected with SARS-CoV-2 and to analyze local epidemiological features.

DESIGN AND SETTING: An observational retrospective study performed using data originated from an official electronic platform for confirmed cases of SARS-CoV-2 infection in humans.

METHODS: We extracted data from patients based in the State of Pernambuco registered in the Center for Strategic Information in Health Surveillance Platform, from February 26 to May 25 2020. Clinical signs/symptoms, patients' evolution with time, distribution of confirmed, recovered and fatal cases and relationship between age group and gender were assessed.

RESULTS: We included 28,854 positive patients for SARS-CoV-2 infection (56,13% female), with median age of 44.18 years old. SARS-CoV-2 infection was more frequent among adults between 30-39 years old and, and for those who progressed to death, the most frequent age range was between 70 and 79 years old. Overall, the mortality rate in the cohort was 8.06%, recovery rate was 30.7% and 17.3% of patients required hospital admission until the end of follow-up. The average time between the symptom's onset and death was 10.3 days. The most common reported symptoms were cough (42.39%), fever (38.03%), and dyspnea/respiratory distress with O_2 saturation < 95% (30.98%).

CONCLUSION: Cough, fever and dyspnea/respiratory distress with oxygen saturation < 95% were the most common symptoms, the case-fatality rate was 8.06%, while hospitalization rate was 17.3%.

INTRODUCTION

The novel ongoing severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has been associated with more aggregated and rapid deaths than previously leading mortality causes, such as unintentional injuries, stroke and heart diseases. As July 6, 2020, more than 11,495,412 confirmed cases have been reported, as well as more than 535,185 deaths have been officially notified.[1] In developing countries, specific data regarding incidence, local clinical manifestation, radiological and laboratory abnormalities as well as requirements for the establishment of a differential diagnosis considering local peculiarities still remains obscure and is often insufficient. In Brazil, for June 15, 2020, 1,603,055 cases and 64,867 deaths have been legally counted.[1]

So far, according to studies from developed countries, typical signs and symptoms of the novel 2019 coronavirus are fever, cough (with or without sputum), sore throat, and shortness of breath (associated or not with respiratory distress with oxygen saturation < 95.0%).[2,3] However, new symptomatic profiles have been described on the literature, mostly on a daily basis. Manifestations as acute olfactory disorders, acute hyposmia and anosmia, dysgeusia as well as dermatological complaints might also be present with the onset of COVID-19.[4-7] Albeit several studies have already described patient's symptomatic profile in European and Asian-Pacific countries, at present there is no study of detailed information for the Brazilian populational setting. Indeed, few publications have been recorded for developing and poor or middle-income

countries. Additionally, the studies for developing settings are either case series, typically with less than 100 patients or are case reports, which shares a narrowed review from a certain topic.[8-10] None of these studies assessed the most common clinical presentations of the novel coronavirus in Brazilian patients, neither attempted to investigate differences of clinical presentation as well as underlying diseases of patients infected with this novel virus.

OBJECTIVE

In this study we aimed to assess the clinical features of Brazilian patients infected with SARS-CoV-2 as well as to analyze patient mortality and the need of hospital admission.

METHODS

Study design

This is an observational retrospective study, based on individual data of Brazilian patients collected from the Center for Strategic Information in Health Surveillance of the Health Secretariat (Ministry of Health, Brazil). This government branch targets early detection, an establishment of a continuous monitoring and delivery of adequate solutions to public healthcare emergencies, as COVID-19. Ethical approval was obtained from a local commission of ethics (reference number 30350820.5.0000.0008), approved on April 13, 2020. The study authors did not have any contact with the patients here described neither delivered any pharmacological or non-pharmacological intervention on them.

Settings

All confirmed patients included in this study were admitted either to primary care centers, private clinics or hospital facilities in the State of Pernambuco (Northeastern Brazil). In accordance to official governmental reports, as June 10, 2020, the State of Pernambuco ranked as the seventh State with more confirmed cases in Brazil (41,010 accumulated cases).[11] Overall, with a total area of 98,311 square kilometers, Pernambuco has about 8.8 million inhabitants, and in 2017 was considered to have a medium human development index (0.67).[12,13] However, due to regional discrepancies inside the State regarding the access of education, life expectancy and per capita income, it is worthwhile mentioning that several composing cities in the State have a low human development index (< 0.50).

Participants

From February 26 to May 25 2020, all patients, regardless age, who presented to any healthcare facility (public or private) with suspect of SARS-CoV-2 infection and were registered into the government online platform of suspected cases were eligible for study inclusion. Regarding the platform interface, patients are enrolled as "suspected cases – under investigation" and as soon the laboratory result is shared with the incoming healthcare center, the designated medical provider can update the patients' status to "negative SARS-CoV-2 infection" or "positive SARS-CoV-2 infection", based on the real-time quantitative polymerase chain reaction (RT-qPCR) report. There is also the possibility to provide results from alternative investigated infections (such as Influenza A or B). In our study, only confirmed patients with SARS-CoV-2 were included in the descriptive analysis. Therefore, patients were excluded if they had a negative laboratory result for SARS-CoV-2. All patients infected tested positive for SARS-CoV-2 by use of RT-qPCR on samples from nasopharyngeal or oropharyngeal specimens. Informed consent was not required because we used secondary data from an official database. The eligibility criteria for the infection diagnosis of SARS-CoV-2 was that at least one gene region was recognized and amplified to be positive for viral proteins (nucleocapsid and open reading frame). The RT-qPCR assay was performed either in the Central Public Health Laboratory (LACEN) or in private diagnostic laboratories.

Variables and outcomes

The main primary variable of the study was the clinical manifestations of patients infected by SARS-CoV-2, along with the categorization of these patients according to the momentary outcome (i.e., until the end of follow-up, on May 25, 2020). Consequently, enrolled patients were classified into five classes of outcomes. Patients with a definitive clinical status were stratified into "Recovered" (patients who after medical assessment were considered without an active infection) and "Died" (patients who progressed to death) subgroups and were compared to each other. Similarly, those individuals with a transient clinical status (waiting for a case improvement or worsening), were categorized into "Domestic quarantine" (patients who were directed to home isolation), "Admitted to hospital care" (patients who, at May 25, 2020, were

hospitalized in an isolation ward or in a regular hospital bed), and "Admitted to intensive care unit (ICU)" (patients who on May 25, 2020, were hospitalized in an ICU).

Exploratory variables such as the distribution of cases according to age group and gender, temporal distribution of included cases, as well as time between the notification and death, time between symptoms onset and death were also analyzed.

Data sources and measurements

In Brazil, a country with both single- and multi-payer system (public and private health care system, respectively), the notification of all SARS-CoV-2 confirmed cases (clinically classified as influenza-like syndrome or severe acute respiratory syndrome) has become mandatory since March 2020 and are registered in online servers and posteriorly processed. The notification and data registration are performed by health care personnel and once the laboratory result is disclosed to the medical facility, the designated medical provider can update the diagnosis status in the system. Influenza-like illness is defined as febrile sensation or fever, associated with cough OR sore throat OR running nose OR shortness of breath, while severe acute respiratory syndrome is defined as influenza-like symptoms with dyspnea/respiratory distress OR persistent thoracic pressure OR oxygen saturation < 95% in ambient air OR peripheric cyanosis. For non-hospitalized patients, such as patients from primary care sector or private clinics, the "e-SUS VE" is the final receptor for all suspected cases. On the other hand, severe acute respiratory syndrome cases and deaths ought to need to be notified through the Information System of Influenza Epidemiological Surveillance (SIVEP-Gripe). In the State of Pernambuco, potentially the most transparent State of Brazil with regards to data sharing and epidemiological surveillance, reports from both systems are periodically integrated and compiled into a single online platform.[13]

All data associated with clinical symptoms and signs, previous health history, and epidemiological features were extracted from the electronic panel of cases of novel coronavirus infection in the State of Pernambuco, Brazil. Two experienced medical research specialists reviewed and abstracted the data. After initial processing, data were entered into a computerized database (Microsoft SQL Server, version 2019, United States of America) and cross-checked.

Study size and statistics

No formal sample size calculation was carried out because of the observational and convenience sampling nature of the study. Statistical evaluation included descriptive analysis for the study population, as well as comparison between groups using chi-square test. We defined a significant statistical different if P-value was < 0.05. Categorical variables were expressed as number and its respective percentage. IBM SPSS, version 20.0 was used to obtain mathematical evaluations.

RESULTS

Characteristics of participants

Overall, 54,235 patients were retrieved in the governmental database up to May 25, 2020. Of these, 28,854 patients had a confirmed laboratory diagnostic for SARS-CoV-2, 22,034 were negative for viral detection and 3,347 were waiting for laboratory result.

From the study sample (N = 28,854), the median age was 44.18 years old, and 56.13% were female, with a male to female ratio of 0.78. The majority of infected patients aged between 30 and 39 years old (N = 6,949, 24.08%). Information regarding underlying diseases was not described for all patients, and it was not possible to know which patients did not have underlying diseases and in which ones there were missing variables. For those patients which any description of preexisting comorbidities, hypertension (N = 863), diabetes (N = 533), obesity (N = 110), chronic renal failure (N = 90), history of stroke (N = 85) and asthma (N = 63) were the most prevalent ones. From the included patients, 22 (0.07%) were classified as having an additional ongoing viral co-infection (either Influenza A or Influenza B) by the time of the notification.

Descriptive data

After distribution of patients into definitive outcomes, 8,863 (30.7%) patients were considered to be recovered of the infection and 2,328 (8.06%) individuals died due to complications of the infection. Male patients were more likely to evolve to death (55.0%) (**Table 1**). For both genders, the majority of fatalities occurred in the group of patients older than 60 years old. In the female group, the majority of deaths were in individuals older than 80 years old, while for male individuals, patients aged between 60 to 69 years old progressed to death more frequently. Regarding patients who recovered, females were more frequent than males (62.63%).

Regarding transient (momentary) outcomes, 4,771 (16,5%) individuals were admitted to an isolation ward, 1,442 (5,0%) were directed to domestic quarantine and 227 (0.78%) were hospitalized in an intensive care unit. In 10,996 confirmed patients with SARS-CoV-2 infection (38%), the final outcome was not available or not declared.

In the overall cohort of confirmed patients, the median time from symptoms onset and notification was 7.0 (IQR 4.0-10.0) days. Among patients who progressed to death, the median time between the symptoms onset and the regulatory notification was of 5.0 (IQR 3.0-8.0) days, whilst the median time between symptoms onset and death was of 8.0 (IQR 5.0-14.0) days.

Analysis of clinical characteristics of confirmed cases of SARS-CoV-2

Summary of clinical manifestations of the 28,854 confirmed cases of infection with SARS-CoV-2 is shown in **Table 2**. Overall, any sign or symptoms were registered in 17,631 patients (61.10%). Thus, 38.9% (N = 11,223) of confirmed patients were notified and registered in the database, but no clinical information was adequately inserted. Patients showed clinical manifestation of cough (with or without sputum) (42.39%), fever (38.03%), dyspnea or respiratory distress with oxygen saturation lower than 95% (30.98%), sore throat or odynophagia (16.79%), myalgia (4.90%), and headache (3.63%). Less common symptoms such as anosmia (2.77%), adynamia or asthenia (1.88%), dysgeusia or loss of taste (1.6%), and hyporexia (0.047%) were also reported

Comparing patients who recovered with those who died, dyspnea or respiratory distress with oxygen saturation < 95% (29.0% versus 88.0%) and fever (59.0% versus 64.0%) were significantly more frequent in patients who died. Sore throat was more frequent in the ones who recovered (39.0 versus 9.0%). When comparing patients hospitalized in isolation ward with patients in ICU, fever (67.0 versus 60.0%) was significantly more frequently observed in those patients in an isolation ward. With regards to patients admitted to ICU, there was a higher frequency of manifesting dyspnea in those patients in the ICU in comparison to those in an isolation ward (74.0 versus 87.0%).

Hypertension, diabetes and obesity were more frequently reported among patients admitted to ICU and the ones who died. A complete description of underlying diseases observed in the included patients, as well as the comparison between patients who progressed to death (case-fatalities) and patients who recovered; and the comparison between patients who were

admitted to isolation ward and those admitted to ICU for each symptom and comorbidity is shown in **Table 2**.

DISCUSSION

Over the last number of weeks, Brazil has become the epicenter of the novel coronavirus pandemic.[14-16] With the global impact of novel coronavirus, it is important to highlight that different populations can manifest different clinical symptoms along with progress differently throughout the natural course of the infection. Overall, the most common reported clinical features were cough (with or without sputum) (42.39%), fever (38.03%), dyspnea or respiratory distress with oxygen saturation lower than 95% (30.44%). Our results showed a slightly lower prevalence's for most observed clinical features as well as for comorbidities compared to previous studies.[3] Severe illness (defined as patients requiring hospitalization) occurred in 17.3% of the patients. Indeed, fever and dyspnea were remarkably more reported among fatalities. In addition, dyspnea and oxygen saturation < 95% showed to be a contributing factor for admission to the ICU. With regards to underlying diseases, the most registered comorbidities were hypertension, diabetes, obesity, and chronic renal failure. Additionally, taking into account underlying pathologies, we observed an association between the presence of comorbidities and a worse progress of the disease. Considering the co-existence of underlying conditions, we perceived that the frequency of comorbidities was slightly less frequent in the reported cases compared to previously published data.[2] However, this might be mainly caused by the singularities of the hospital environment and the emergency department features, where very frequently a detailed medical history obtention is not possible to be implemented.

Even though the disease profiling has been replicated and performed in several countries, this is the first study to describe, using a considerable number of patients, the main clinical characteristics and outcome distribution in Brazil. Brazil, a country with continental geographic proportions, has a wide spectrum of tropical infectious diseases (most of them neglected), such as Chagas disease, leishmaniosis and dengue. However, to date, no previous diseases has had the impact of abruptly increasing the number of patients seeking medical consultations.[17] Associated to its large territory proportions, Brazil is also a social and economically inequal country, which consequently interferes in the health status of its inhabitants.[18] Thus, as the novel coronavirus

disseminates across the country, the impact of the disease on low-income populations negatively increases.

The extensive spectrum of reported symptoms during admission (with several body systems being involved), summed to wide a range of severity (from asymptomatic cases to severely ill patients), may potentially cause an initial misdiagnose, especially for those patients which a first RT-PCR is negative.[4] We identified a low frequency of reports of data on anosmia/hyposmia and other minor symptoms as dermatological manifestations. However, considering that the reporting of these symptoms started on mid-April, the medical attention for these manifestation in our cohorts might be delayed or with less attention in Brazilian settings. Nevertheless, several studies have already described the high sensitivity feature of these particular symptoms on the disease diagnosis.[4] In addition, developing countries, as Latin American and African countries, have their own endemic diseases, in current ascending numbers, in which challenges even more the conclusion of a final diagnostic hypothesis.[19] Fever was more prevalent among those patients who died compared to those who required hospital admission. However, we hypothesized that this might be due to lack of complete fulfillment of the reporting questionnaire, which cause a less frequency among those patients who needed hospital care. In our study, the majority of the symptoms could be associated to alternative infections, such as influenza, rhinovirus, dengue fever or gastroenteritis. Therefore, we highlight the fact that in those areas where co-existing outbreaks might be occurring in parallel, a differential diagnosis should always be in mind, in order to rule out potential secondary pathogens and to prompt a more accurate clinical management for patients who a differential diagnosis could not established yet.

In our study, 8% (N = 2,328) of patients with SARS-CoV-2 infection progressed to death (in less than three months). The mortality rate in the State of Pernambuco was also slightly higher than the national Brazilian average, possibly because of the economic peculiarities of the region and because of lack of hospital infrastructure for severe cases.[20] In addition, possible explanations for this higher mortality rate can be related to a delayed diagnosis of the disease (fundamentally caused by laboratory and trained medical personnel limitation) or even patients' fear to seek medical care in the early stage of the pathology, which, as a consequence, favors a more severe involvement during late hospital admission. In addition, in the State of Pernambuco, a significant number of municipalities face either geographical or structural difficulties for the

access of appropriate medical treatment. A compelling example of these challenges is that, by the period analyzed (May 25, 2020), 98% of available beds for COVID-19 patients (isolation wards or ICU) were occupied. Thus, the relevance of the disease, in special in settings where social and economic discrepancies prevails, is of utmost importance. Although this number might be underestimated, SARS-CoV-2 represents an important public health care issue in Brazil and in developing countries across the globe. Taking into account the entire year of 2018 (when the total number of deaths in the State of Pernambuco was 62,011 deaths), this number corresponds the same mortality rate for all infectious diseases aggregated (including flu, tuberculosis, any hepatitis, and HIV).[20] Considering the body of literature, the mortality rate observed in our study is slightly higher when compared to different settings as China and Italy.[20-23]

Our data suggested a higher mortality rate between Brazilian male subjects in comparison with Brazilian female individuals, which is also observed in previous studies.[3] Even though it was perceived that female patients had 56.0% of the total number of confirmed infections, there was a higher mortality rate among male patients (55.0%). There are different hypothesis to explain this fact. Initially, it has been suggested that women might be less susceptible to viral infections than men due to a higher production of circulating antibodies along with a prolonged level of these biomarkers.[22,23] Additionally, another factor that can explain a less susceptibility of female patients to the novel coronavirus infection is the production of estrogen and immune factors linked to X chromosomes.[24] In women, the double X chromosome affects the immune system on expression of several elements, such as the expression of Toll-like 7 receptor (TLR7).[25] Once the TLRs are higher expressed in women and its expression leads to higher immune responses, it has been suggested that these two associated factors might therefore increase resistance to viral infections. Another cellular related explanation for a higher immunoprotection of female patients over male patient is associated with the CD4+ T cells.[26] With a higher expression in women individuals, a state of higher immune response may be achieved in female patients in comparison to men, providing also a more protective status.[25,26] Lastly, but not least, cultural features can also account for the imbalanced mortality rate between male and female patients. In Brazil, the promotion of health policies for women, make this population closer to healthcare facilities (for elective medical procedures or for emergencies).[27,28] In addition, especially in traditional areas as the Northeast of Brazil, the stereotype of the masculine image, which represents the family progenitor who never gets sick, can also be related

to this sociocultural aspect.[20,30] Thus, even with disparities of confirmed cases between male and females, male patients are at higher risk for a fatal outcome as compared to female individuals.

The main strength of the current study was to analyze more than 28,000 patient's data of laboratory confirmed individuals, excluding, therefore, those patients who are frequently clinically diagnosed only, and thus may be infected with other diseases instead. Moreover, we included patients from different municipalities of the State of Pernambuco, which gives us a more heterogeneous dataset, as well as a more representative and less biased sample selection. Essentially, the main limitation of the study regards to those patients admitted to either isolation wards or to intensive care unit. Furthermore, another worthwhile limitation to be mentioned regards to the fact that during the admission to emergency departments the complete fulfillment of the notification sheet might be compromised. This is because the high demand (several incoming patients hourly), insufficiency of medical personnel and also the presence of severe cases, which requires more attention. Additionally, the data entry from multiple locations and professionals causes an inherent contrast on the use of medical terms and description, which also results in a heterogeneity of fulfilment. Therefore, a most complete and accurate medical history (including information about underlying diseases and a more detailed description of symptoms) is sometimes not possible to be achieved. However, we believe that for health decision-makers and medical researchers, a framework of the current pandemic situation is of utmost importance, in order to understand more specifically the Brazilian scenario.

CONCLUSION

The novel coronavirus has been affecting developing countries as Brazil dramatically. In Brazil, the disease has been shown to have a broad gamut of symptoms and severity, including common symptoms such as cough, fever, dyspnea and sore throat. Considering the overall all-cause mortality of 8.06%, it is important that preventive non-pharmacological interventions are endorsed by health authorities until a vaccine is safe and universally available. Taking the statistical difference between patients who progressed to death and those who recovered, medical providers should consider the presence of dyspnea or respiratory distress with oxygen saturation < 95% and fever as an important prognosis factor. We emphasize the importance of mandatory reporting systems in terms of better understanding the distribution and evolution of infectious diseases in Brazil and recommend that a better and complete medical history investigation and

reporting should be implemented in medical units across the country. At present times, international researcher should focus their efforts with high-quality studies assessing the effectiveness of the most used pharmacological and non-pharmacological interventions, besides the multiple ongoing immunization therapies trials.

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Table 1. Age distribution of the retrieved data

Age range (by group)	Confirmed cases (N = 28,854) N (%)		Recovered cases (N = 8,863) N (%)		Case-fatalities (deaths) (N = 2,328) N (%)	
	Female	Male	Female	Male	Female	Male
0 to 9 years old	444 (1.53)	373 (1.29)	156 (1.76)	140 (1.56)	6 (0.25)	5 (0.21)
10 to 19 years old	178 (0.61)	143 (0.49)	42 (0.47)	36 (0.40)	4 (0.17)	4 (0.17)
20 to 29 years old	2,018 (6.99)	1,262 (4.36)	764 (8.62)	408 (4.60)	14 (0.60)	15 (0.64)
30 to 39 years old	4,171 (14.45)	2,778 (9.62)	1,768 (19.95)	926 (10.43)	24 (1.03)	54 (2.32)
40 to 49 years old	3,717 (12.88)	2,861 (9.91)	1,509 (17.02)	882 (9.94)	60 (2.57)	127 (5.46)
50 to 59 years old	2,552 (8.84)	2,098 (7.26)	886 (9.99)	546 (6.15)	150 (6.44)	179 (7.69)
60 to 69 years old	1,325 (4.59)	1,376 (4.75)	237 (2.68)	208 (2.34)	246 (10.57)	315 (13.54)
70 to 79 years old	947 (3.28)	1,059 (3.66)	102 (1.16)	98 (1.10)	258 (11.09)	312 (13.40)
> 80 years old	846 (2.93)	706 (2.43)	87 (0.98)	68 (0.75)	286 (12.29)	269 (11.56)
Total	**16,198 (56.13)**	**12,656 (43.87)**	**5,551 (62.63)**	**3,312 (37.37)**	**1,048 (45.01)**	**1,280 (54.99)**

Notes:

* = confirmed co-infection is either for Influenza A or Influenza B.

During the analyzed period, there were 54,235 cases registered in the database (including suspected, confirmed and negative cases).

Table 2. Clinical data from confirmed cases of SARS-CoV-2 infection in the State of Pernambuco, Brazil (data up to May 25, 2020)

Clinical presentation of confirmed patients (N = 17,631)	Domestic quarantine (N = 1,442) N (%)	Recovered (N = 8,863) N (%)	Case-fatalities (N = 2,328) N (%)	Admitted to isolation ward (N = 4,771) N (%)	Admitted to ICU (N = 227) N (%)	Comparison between recovered and case-fatalities patients (P-value)	Comparison between patients admitted to isolation ward and ICU (P-value)
Cough (N = 12,232)	874 (0.60)	6,124 (0.69)	1,574 (0.67)	3,512 (0.73)	148 (0.65)	0.169	0.005
Fever (N = 10,976)	853 (0.59)	5,256 (0.59)	1,493 (0.64)	3,236 (0.67)	138 (0.60)	< 0.001	0.027
Dyspnea or respiratory distress with SpO_2 < 95% (N = 8,941)	507 (0.35)	2,619 (0.29)	2,057 (0.88)	3,559 (0.74)	199 (0.87)	< 0.001	< 0.001
Sore throat or odynophagia (N = 4,847)	460 (0.31)	3,470 (0.39)	216 (0.09)	664 (0.13)	37 (0.16)	< 0.001	0.313
Myalgia (N = 1,416)	460 (0.31)	333 (0.03)	99 (0.04)	513 (0.10)	11 (0.04)	0.270	0.005
Vomiting or nausea or diarrhea (N = 1,293)	186 (0.12)	316 (0.03)	191 (0.08)	582 (0.12)	18 (0.07)	< 0.001	0.053
Headache (N = 1,049)	277 (0.19)	352 (0.03)	51 (0.02)	361 (0.07)	8 (0.03)	< 0.001	0.023
Anosmia (N = 801)	223 (0.15)	284 (0.03)	31 (0.01)	257 (0.05)	6 (0.02)	< 0.001	0.070
Adynamia or asthenia (N = 545)	55 (0.03)	120 (0.01)	77 (0.02)	287 (0.06)	6 (0.02)	< 0.001	0.035
Dysgeusia or loss of taste (N = 490)	170 (0.11)	218 (0.02)	20 (< 0.01)	77 (0.01)	5 (0.02)	< 0.001	0.495
Hyporexia (N = 138)	10 (< 0.01)	10 (< 0.01)	31 (0.01)	85 (0.01)	2 (< 0.01)	< 0.001	0.311
Abdominal pain (N = 88)	7 (< 0.01)	13 (< 0.01)	19 (< 0.01)	48 (0.01)	1 (< 0.01)	< 0.001	0.398
Sneezing (N = 46)	9 (< 0.01)	27 (< 0.01)	1 (< 0.01)	9 (< 0.01)	-	0.025	0.512
Eye pain (N = 20)	5 (< 0.01)	16 (< 0.01)	2 (< 0.01)	3 (< 0.01)	-	0.724	0.705
Chest pain (N = 12)	3 (< 0.01)	4 (< 0.01)	1 (< 0.01)	4 (< 0.01)	-	0.965	0.663
Running nose (N = 9)	4 (< 0.01)	154 (0.01)	19 (< 0.01)	2 (< 0.01)	-	< 0.001	0.758
Asymptomatic (N = 9)	1 (< 0.01)	5 (< 0.01)	1 (< 0.01)	2 (< 0.01)	-	0.803	0.758
Not declared or not available (N = 1,339)	279 (0.19)	704 (0.07)	107 (0.04)	239 (0.05)	10 (0.04)	< 0.001	0.683
Comorbidities							
Hypertension (N = 863)	17 (0.01)	63 (< 0.01)	643 (0.27)	126 (0.02)	14 (0.06)	< 0.001	0.002

Diabetes (N = 533)	1 (< 0.01)	182 (0.02)	309 (0.13)	35 (< 0.01)	6 (0.02)	< 0.001	0.002
Obesity (BMI > 25kg/m^2) (N = 110)	1 (< 0.01)	6 (< 0.01)	86 (0.03)	14 (< 0.01)	3 (0.01)	< 0.001	0.009
Chronic renal failure (any stage) (N = 90)	-	2 (< 0.01)	76 (0.03)	11 (< 0.01)	1 (< 0.01)	< 0.001	0.528
History of stroke (N = 85)	-	2 (< 0.01)	72 (0.03)	10 (< 0.01)	1 (< 0.01)	< 0.001	0.468
Asthma (N = 63)	-	12 (< 0.01)	35 (0.01)	14 (< 0.01)	2 (< 0.01)	< 0.001	0.126
Chronic obstructive pulmonary disease (N = 48)	-	5 (< 0.01)	36 (0.01)	4 (< 0.01)	3 (0.01)	< 0.001	< 0.001
Any neoplasia (N = 33)	-	3 (< 0.01)	26 (0.01)	4 (< 0.01)	-	< 0.001	0.663
History of myocardial infarction (N = 32)	-	1 (< 0.01)	27 (0.01)	3 (< 0.01)	1 (< 0.01)	< 0.001	0.049
Chronic liver disease or hepatitis (N = 11)	-	1 (< 0.01)	5 (< 0.01)	5 (< 0.01)	-	< 0.001	0.626
HIV infection (under control or not) (N = 9)	-	3 (< 0.01)	4 (< 0.01)	2 (< 0.01)	-	0.018	0.758
Transplanted (N = 3)	-	-	2 (< 0.01)	1 (< 0.01)	-	0.006	0.827
Alcoholism (N = 1)	-	-	1 (< 0.01)	-	-	0.051	-
Without comorbidities or not declared or not available (N = 8,308)	866 (0.60)	3,640 (0.41)	767 (0.32)	2,882 (0.60)	153 (0.67)	< 0.001	0.035

Note:

ICU = intensive care unit; BMI = body mass index; HIV = human immunodeficiency virus

It is important to state that the comparison shown above regards to 1) Comparison between patients who progressed to death (case-fatalities) and patients who recovered; and 2) Comparison between patients who were admitted to isolation ward and those admitted to ICU. Therefore, for each symptom and comorbidity category, we performed statistical analysis to check whether there was group-to-group significant difference.