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Prospective Study

Epidemiological and clinical characteristics of COVID-19 in a Brazilian public hospital

Pinheiro FD *et al.* Epidemiological and clinical characteristics of COVID-19

Abstract

BACKGROUND

The coronavirus disease 2019 (COVID-19) pandemic has become a major health concern worldwide. In that context, the understanding of epidemiological and clinical features associated with the disease and its severity is crucial for the establishment of strategies aiming at disease control and remedy.

AIM

To describe epidemiological features, signs, symptoms, and laboratory findings among severely ill COVID-19 patients from an intensive care unit (ICU) in Northeastern Brazil as well as to evaluate predictor factors for disease outcomes.

METHODS

This is a prospective single-center study that evaluated 115 patients, admitted to the ICU in a Northeastern Brazil Hospital.

RESULTS

The patients had a median age of 65.60 ± 15.78 . Dyspnea was the most frequent symptom, affecting 73.9% of the patients, followed by cough (54.7%). Fever was reported in approximately one third and myalgia in 20.8% of the patients. At least two comorbidities have been found in 41.7% of the patients, and hypertension was the most prevalent one (57.3%). In addition, having two or more comorbidities was a predictor of mortality, and lower platelets count was positively associated with death as well. Regarding symptoms, nausea and vomiting were predictors of death and cough was a protective factor.

CONCLUSION

This is the first report of a negative correlation between cough and death in severely ill severe acute respiratory syndrome coronavirus 2-infected individuals. The associations

between comorbidities, advanced age, and low platelets count and the outcomes of the infection were similar to the results of previous studies, highlighting the relevance of these features.

Key Words: COVID-19; Epidemiology; Symptoms; Comorbidities; Laboratory parameters

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Core Tip: This is a prospective study, carried out in a hospital in Brazil, with 115 patients admitted to the intensive care unit with a positive diagnosis for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) to describe epidemiological features, signs, symptoms, and laboratory findings among severely ill coronavirus disease 2019 patients as well as to evaluate predictor factors for disease outcomes. This is the first report of a negative correlation between cough and death in severely ill SARS-CoV-2-infected individuals.

INTRODUCTION

Since its first records at the end of 2019 in Wuhan, capital city of Hubei province, China, the coronavirus disease 2019 (COVID-19) has risen numerous challenges with regard to a better understanding of its immunology, pathophysiology, clinical manifestations, diagnosis, and treatment^[1]. The pathogen was identified as a novel enveloped RNA betacoronavirus that has a phylogenetic similarity to the severe acute respiratory syndrome coronavirus 1 (SARS-CoV-1). In that context, the so-called SARS-CoV-2 has become a global health concern and, on March 11, 2020, the World Health Organization

has declared the COVID-19 outbreak a pandemic^[2]. The incubation period for COVID-19 is generally within 14 d following exposure, and the onset of symptoms occurs more often four-to-five days after inoculation^[3]. In a study including 1084 COVID-19 patients from China, the median period of incubation was 7.8 d, with 5% to 10% of patients experiencing the first symptoms after 14 d of exposure^[3]. Recent meta-analyses about the topic corroborate this finding, highlighting averages of 5.1 and 5.6 d for disease incubation, respectively^[4,5]. Among those affected by the disease, about 17.9% to 33.3% remain asymptomatic, highlighting the difficult control of the transmission of that disease^[6]. Pneumonia is the most frequent serious finding and it usually occurs with fever, cough, expectoration, and dyspnea. Other common symptoms are myalgia, diarrhea, anosmia and dysgeusia, and upper respiratory tract symptoms^[7-9]. Of note, dysgeusia and anosmia disorders are more common in COVID-19 than in other viral infections^[10]. It has to be emphasized that the prevalence of SARS-CoV-2 infection-related manifestations can vary depending on the level of severity of the illness. In this sense, the prevalence of fever was higher among hospitalized patients in a trial with 1099 patients when compared to non-hospitalized COVID-19 patients: Only 44% of the patients had fever at admission, whereas 89% were febrile during hospitalization^[11]. When compared to severe and mild disease groups, patients with moderate involvement have higher rates of dysgeusia and anosmia (88.70% among patients with moderate disease and 45.83% in severely ill individuals)^[12].

As prognostic markers of the disease, clinical and epidemiological features have been reported as predictors of severity among patients in hospital care. While dyspnea is also an important finding for a poor prognosis, studies suggest that peripheral O₂ saturation is the respiratory factor to be assessed, as it excludes the subjective factor from the assessment. These studies suggest that an oxygen saturation below 92% is associated with a poor prognosis. Furthermore, whereas it takes about 5 d for the patient to develop dyspnea after the first symptoms, it can be quickly followed by acute respiratory distress syndrome. In this sense, adequate monitoring of saturation levels in COVID-19 patients is indicated^[13]. Efforts have been directed towards the

understanding of the relationship between comorbidities and the severity and mortality in SARS-CoV-2 infection. In this sense, studies have shown that diabetes, hypertension, obesity, and cardiovascular disease are important risk factors for severity and mortality^[14-16]. In addition, various abnormalities in serum laboratory parameters have been associated with the COVID-19, and some of them have been related to an increased risk of mortality^[17,18]. To date, SARS-CoV-2 has infected almost 200 million people worldwide, from which 4 million died^[2]. In Brazil, 30639130 cases of the disease have been registered so far, with 664641 deaths associated with the disease. The Northeast region of Brazil, in which the current study was carried out, the disease was responsible for 6256874 cases, with the occurrence of 128829 deaths among them^[19]. Given the above, the aim of this study is to describe epidemiological features, signs, symptoms, and laboratory findings at the moment of intensive care unit (ICU) admission among severely ill COVID-19 patients in a city from Northeastern Brazil as well as to evaluate predictor factors for disease outcomes in the study sample. This study shows some differences in the clinical and epidemiological profiles of COVID-19 patients when compared with previous studies, mainly regarding the frequency of symptoms. We report, for the first time, a negative association between cough and death among severely ill SARS-CoV-2-infected patients.

MATERIALS AND METHODS

Study design and participants

This single-center prospective study included 225 consecutive COVID-19 patients admitted to the ICU, General Hospital of Vitória da Conquista city, Bahia State, Brazil, from July 30, 2020 to August 28, 2021. The Vitória da Conquista General Hospital is a regional hospital in the third largest city in the Bahia State, providing an extensive multidisciplinary teaching service, which attends to a large number of highly complex cases from more than 70 surrounding cities. All included patients had SARS-CoV-2 infection confirmed by real-time polymerase chain reaction (RT-PCR) of nasopharyngeal swab specimens. Subjects were selected according to the criteria for

ICU admission recommended by the Bahia State Department of Health. This study was approved by the Ethics Committee of the Brazilian National Research Ethics Commission (No. 4.155.234), with an informed consent form obtained from the relatives responsible for the enrolled patients.

Data collection

Epidemiological, clinical, and laboratory data of the included patients were obtained both at admission and during hospitalization. Clinical outcomes were monitored in the inpatient system, which indicated discharge, transfer or death. Data collection comprised clinical, epidemiological and demographic data, as well as exposure history to infected individuals, date of symptom onset, RT-PCR result and presence of comorbidities. Comorbidities included: (1) Hypertension; (2) Diabetes; (3) Cardiovascular disease; (4) Chronic kidney disease; (5) Obesity; (6) Chronic obstructive pulmonary disease (COPD); and (7) Autoimmune diseases. Blood samples were obtained from the patients for assessment of white blood cells [mm^3 ; reference values: $(4-10) \times 10^3$] and platelets [g/L , reference values: $(150-450) \times 10^3$] count, hemoglobin levels [mg/dL ; reference values 11.5-18.0 (female) or 13.0-18.0 (male)], C-reactive protein (CRP: g/L ; reference value: ≤ 6), serum sodium (mEq/L ; reference values: 130-150), aspartate aminotransferase (AST - U/I ; reference values: 10-37), alanine aminotransferase (ALT - U/I ; reference values: 10-45) and lactic dehydrogenase (U/I ; reference values: 120-246). All laboratory evaluations were done by conventional methods. Statistical analysis data were analyzed by the public domain statistical software Epi Info 7 and the SPSS statistical software package version 26.0 (SPSS Inc., Chicago, IL). For the comparisons, Kolgomorov-Smirnov or Shapiro-Wilk test were used to assess the normality of the data as indicated. Two-tailed student's t test or Mann-Whitney U test as well as χ^2 test with Yates' correction or Fisher's exact test were employed as indicated. The level of significance was set at $P \leq 0.05$. Forward binary logistic regression was performed during analysis.

RESULTS

Demographic data

All subjects were positive for SARS-CoV-2 RNA detected by RT-PCR. Their mean age (standard deviation - SD) was 65.60 ± 15.78 . Patients included 69 (60%) males (mean age = 67.09, SD = 14.09) and 46 (40%) females (mean age = 63.37, SD = 17.96). A total of 38 patients (33.1%) were from Vitória da Conquista and 36 from adjacent cities.

Clinical features

The most frequent clinical symptom was dyspnea, present in more than two thirds of the included patients (85 patients - 73.9%). Cough was the second most frequent symptom (63 patients - 54.7%) followed by fever (38 patients - 33%), myalgia (24 patients - 20.8%), diarrhea (9 patients - 7.8%), nausea (8 patients - 6.9%), vomiting (7 patients - 6.0%), headache, dysgeusia and anosmia (5 patients - 4.34% in each). Regarding comorbidities, 66 patients (57.3%) had hypertension, 32 (27.8%) had diabetes, 23 (20%) had cardiovascular disease, 15 (13%) had obesity, 12 (10.4%) had chronic kidney disease, 4 (3.4%) had COPD and 1 (0.8%) had autoimmune disease. In the group of patients from whom the information was obtained, no comorbidities were present in 15 patients, whereas 36 and 29 had 1 and 2 comorbidities, respectively. The others had either 3 ($n = 13$) or 4 ($n = 5$) comorbidities.

Vital signs and laboratory data

Respiratory rate was increased in the majority of patients ($n = 39$; 52%), whereas 2 patients (2.7%) presented with bradipnea and 34 individuals (45.3%) were eupneic. Regarding laboratory data, the white blood cell count was elevated in 61.9% of the patients ($n = 60$) and leucopenia was observed in 5 (5.2%) individuals (reference value = 5000-11000 leucocytes/mm³). The inflammatory marker CRP was found to be altered in 74 patients (96.10%; reference value ≤ 3 mg/L). Regarding hepatic lesion markers, AST and ALT levels were elevated in 13 (54.2%) and 15 (68.2%) of the participants, respectively. When the groups of patients who died were compared with those who

had a favorable disease outcome, increasing age was significantly associated with death (69.28 ± 15.16 vs 61.54 ± 17.08 , $P = 0.02$). The presence of two or more comorbidities was a positive predictor of mortality ($P = 0.01$). The presence of at least two concomitant illnesses was observed in 60.9% of the patients who died, compared with the other group (39.1%). No association was observed with the gender (female, male, $P = 0.16$) a plethora of patient factors-including demographic, clinical, immunologic, hematological, biochemical, and radiographic findings - that may be of utility to clinicians to predict COVID-19 severity and mortality. In addition, the mean platelet count among patients who died was 141.49×10^3 g/L. A statistically significant relationship was observed between the lower platelet count and death ($P \leq 0.001$). No statistically significant results were obtained when other comorbidities and laboratory results were assessed.

Association between symptoms and clinical outcomes. When evaluating the main outcomes and the symptoms of the patients on ICU admission, we found that nausea ($P = 0.02$), and vomiting ($P = 0.05$) were predictors of death and that cough was a protective factor. There was no statistically significant association between other symptoms and the evaluated outcomes (Table 4).

DISCUSSION

This study evaluated the clinical and epidemiological profiles of hospitalized individuals from an ICU in a Brazilian public hospital. Regarding the symptoms, some data found in this investigation diverge from the pattern observed in previous studies. In an investigation in China, fever was the most prevalent symptom among the 1099 laboratory-confirmed COVID-19 patients at admission (43.8%) or during hospitalization (88.7%)^[20], in contrast to the approximately one third observed in our patients. Furthermore, a high prevalence of fever (88.7% of the 656 patients) was also identified in a meta-analysis study^[21].

Notably, cough was not associated with poor outcomes among the severely ill COVID-19 patients we evaluated. To the best of our knowledge, this is the first study to

demonstrate a negative association between cough and death in patients infected with SARS-CoV-2 in ICU, in contrast to the observed in a meta-analysis study evaluating 10014 patients with COVID-19^[22]. In addition, a high prevalence of this symptom was observed in the present study, corroborating an investigation from the Center for Disease Control and Prevention (CDC), which evaluated 373883 individuals and found that the aforementioned symptom was the most common manifestation in COVID-19 (50%)^[23]. Seeking explanations for this finding, the hypothesis of coughing as an alarm signal was raised. This sign would make patients seek emergency care earlier when compared to critically ill patients without cough. Probably the patients without cough but desaturation and severe condition did not understand that they should be evaluated by a doctor. During the peak of the epidemic, health systems were overcrowded and government entities were even oriented on a national network to seek assistance only in a serious condition. Faced with this sum of situations, we may be dealing with a needy population, with low availability of health services and with government guidelines to avoid emergency services, culminating in critically ill patients staying at home and probably arriving at hospitals in very serious conditions. This could also explain the study's high mortality rates. Otherwise, nausea and vomiting were positively associated with death in the present study in contrast to previous investigations that have associated gastrointestinal symptoms with milder SARS-CoV-2 infections. The frequency of gastrointestinal symptoms found here was lower than in other surveys. In a systematic review performed by our group that included 43 studies and 18246 COVID-19 patients, the prevalence of diarrhea was higher than in this investigation^[8]. The most common symptom in our investigation was dyspnea, a pivotal finding among severely ill COVID-19 patients. In a meta-analysis study evaluating 1813 patients, only dyspnea was able to predict severe disease and ICU admission^[24]. Headache was more infrequent in our patients than in the aforementioned investigation by CDC^[23] probably because they were admitted to the ICU after the administration of analgesics in the emergency room or in other hospitals. Similarly, there was a low prevalence of anosmia and taste change, which is expected, because these symptoms have been observed in

better prognosis^[21]. Leukocytosis was found in most individuals included in this investigation in agreement with the higher frequencies of this manifestation reported among critically ill individuals^[25,26]. Red blood cell count abnormality was another relevant laboratory finding in this study, with the detection of hemoglobin levels below 11 g/dL in 38.7% of the patients in accordance with previous studies showing reduced levels of serum hemoglobin in SARS-CoV-2-infected individuals with severe disease^[21]. The levels of serum lactate dehydrogenase were found to be increased in our sample, a common finding among COVID-19 patients^[27]. Moreover, serum sodium levels were increased in the patients we evaluated, similarly to the increased odds of in-hospital death among hypernatremic individuals compared to normonatremic persons^[28]. Furthermore, lower platelets count was positively associated with mortality in our investigation. Previous studies suggest that the occurrence of thrombocytopenia in SARS-CoV-2 infection can be associated with serious conditions such as intravascular coagulation and sepsis^[29]. Other causes of low platelets count in COVID-19 stand out drug-induced have been suggested^[3]. This study demonstrated a higher mortality rate among critically ill SARS-CoV-2-infected individuals than most studies did. Of note, ICU mortality due to COVID-19 around the world has ranged from 20% to 62%^[30-32]. It has to be emphasized the difficulties faced by the Brazilian public health system to make enough ICU beds available for COVID-19 patients during the aforementioned pandemics. In the period from 2020 to 2021, there were approximately 70 ICU beds in the study city, which is the main healthcare center in a region that embraces 2 million inhabitants^[33]. This scenario predisposed the occurrence of delays in providing adequate life support for critically ill individuals, which potentially contributed to the high mortality rate observed in this study. A high prevalence of comorbidities was observed in our patients. Hypertension was the most prevalent comorbidity in agreement with a meta-analysis study. Moreover, the presence of 2 or more comorbidities as well as older age were associated with higher mortality in our study, results similarly to previous studies^[34]. The circulating variants of SARS-CoV-2 is an important issue to be taken into account when considering the clinical manifestations of

COVID-19 among individuals from a given geographical area^[35]. Although the differentiation of the SARS-CoV-2 strains that has infected the patients could not be performed in this study, the co-circulation of 13 different strains has been reported to date in the Brazilian state where the study was carried out. The first subline identified was the B.1.1.162^[36]. Of note, the variants P.1 and P.2, which have been identified in the Brazilian cities Manaus and Rio de Janeiro, respectively, have been detected in the aforementioned state as well^[37,38]. Lastly, the Peruvian lineage C.14 was also detected in the study region after its introduction through a ship traveler. Until February 2021, the variants circulating in Bahia state were limited to A, B, C and P types^[39,40]. This was an epidemiological investigation conducted at a single health care system with a limited number of participants and in a confined geographic area, thus limiting the generalizability of the results. ³ Future research should be made to identify and predict further factors associated with mortality in COVID-19 populations admitted to the ICU.

CONCLUSION

This study shows some differences in the clinical profile of COVID-19 patients when compared with previous studies, observing a negative association between cough and death in severely ill individuals. On the other hand, the associations between comorbidities, advanced age, and low platelets count and the outcomes of the infection were similar to the results of previous studies, highlighting the relevance of these features. Further investigations are needed in order to better characterize risks of poor outcomes among severely ill COVID-19 patients.

ARTICLE HIGHLIGHTS

Research background

Since its ascension in 2019, coronavirus disease 2019 (COVID-19) has become a health concern around the world. An understanding of the epidemiological and clinical features related to the infection is very important for the development of ways to prevent and treat the disease.

Research motivation

There is a lack of studies evaluating the clinical and epidemiological characteristics of patients with severe COVID-19 in the study region. Moreover, the data regarding the infection features in that population certainly contribute to the understanding of the disease.

Research objectives

The research had as its objectives the description of epidemiological characteristics, signs, symptoms, and laboratory findings in individuals with severe COVID-19 from an intensive care unit (ICU) in the State of Bahia, Northeastern Brazil, analyzing predictor features for the disease outcomes.

Research methods

In this prospective, single-center study, 115 patients with severe COVID-19 admitted to an ICU in Northeastern Brazil were evaluated. Epidemiological, clinical, and laboratory data of the included patients were obtained. Clinical outcomes were monitored in the inpatient system.

Research results

The patients had a median age of 65.60 ± 15.78 . Dyspnea was the most frequent symptom, affecting 73.9% of the patients, followed by cough (54.7%). Fever was reported in approximately one-third and myalgia in 20.8% of the patients. At least two comorbidities have been found in 41.7% of the patients, and hypertension was the most prevalent one (57.3%). In addition, having two or more comorbidities was a predictor of mortality, and lower platelets count was positively associated with death as well. Regarding symptoms, nausea and vomiting were predictors of death and cough was a protective factor.

Research conclusions

This is the first report of a negative correlation between cough and death in severely ill severe acute respiratory syndrome coronavirus 2-infected individuals. The associations between comorbidities, advanced age, low platelet count, and the outcomes of the infection were similar to the results of previous studies, highlighting the relevance of these features.

Research perspectives

In future analyses, we aim at evaluating the role of various cytokine profiles in the inflammatory response in the population of the study. Moreover, the relationship between comorbidities and infection outcomes might be further explored in the next steps of the research.

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