

FACTORS ASSOCIATED WITH DEATH OF COVID-19 PATIENTS: CASE SERIES

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ABSTRACT

This aim of this study was to identify potential factors associated with survival in patients with coronavirus disease 2019 (COVID-19). This study was designed as a case series. It included patients hospitalized in Clinical Centre Kragujevac between March 10, 2020, and June 15, 2020, due to COVID-19. Variables with significant influence on the cure of patients were identified by multivariate logistic regression. A total of 234 patients were included. The average age of the patients was 57.2 ± 15.8 years. Thirty-five patients died (15.0%) and 199 (85.0%) were discharged as completely cured and with the sustained virological response.

The study variables with significant influence (expressed as odds ratio – OR) on cure of COVID-19 patients after adjustment for effects of other variables were: stay in an intensive care unit – ICU (OR = 0.007; 95% confidence interval – CI 0.001 – 0.086; $p = 0.000$), previous hospitalization (OR = 7.802; 95% CI 1.198 – 50.924; $p = 0.032$), increased body temperature on admission (OR = 0.004; 95% CI 0.000 – 0.771; $p = 0.040$), higher score of the Charlson Comorbidity Index (OR = 0.428; 95% CI 0.235 – 0.780; $p = 0.006$), and increased values of C-reactive protein (CRP) serum level (OR = 0.978; 95% CI 0.966 – 0.990; $p = 0.000$). In conclusion, clinicians should pay attention to patients with high body temperature at admission, presence of multiple comorbidities, high CRP, and patients who stay in an ICU, considering that they could be at risk for fatal outcome.

Keywords: risk factors, death, mortality, COVID-19, SARS-CoV-2.

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ABBREVIATIONS

ALT – Alanine aminotransferase
ARDS – Acute respiratory distress syndrome
AST – Aspartate aminotransferase
CDC – Centers for Disease Control and Prevention
CI – Confidence interval
COPD – Chronic obstructive pulmonary disease
COVID-19 – Coronavirus disease 2019
CT – Computed tomography
HAI – Healthcare-associated infection
ICU – Intensive care unit
MERS – Middle East Respiratory Syndrome
OR – Odds ratio
RT-PCR – Reverse-transcriptase polymerase-chain-reaction
SARS-CoV-2 – Severe acute respiratory syndrome coronavirus-2
SPSS – Statistical Software for Social Sciences

INTRODUCTION

The international community shows a high degree of interest for a cluster of pneumonia cases caused by the new coronavirus, called a severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), since the occurrence of first cases of the disease at the end of December 2019 in Wuhan city, Hubei province, China (1,2). Considering that SARS-CoV-2 was a new virus strain that had not been previously identified in humans, World Health Organization (WHO) designated the disease caused by this virus as a new entity naming it coronavirus disease 2019 (COVID-19) (3).

Coronaviruses are a large group of viruses with low epidemiological significance that cause respiratory infections in humans, with symptoms ranging from the common cold to severe pneumonia. Only members of this group of viruses that were of greater importance were SARS-CoV-1, which appeared in 2002-2003, and Middle East Respiratory Syndrome (MERS), which appeared in 2012, because they led to the outbreak of minor epidemics (4,5). SARS-CoV-2 is the seventh member of the enveloped RNA coronavirus family to infect humans and belongs to subgenus *Sarbecovirus* and subfamily *Orthocoronavirinae* (6–8). It can cause fatal pneumonia, in addition to asymptomatic and moderately severe respiratory tract infections (6–8). Its capability of interhuman transmission and rapid global spread has given it great epidemiological significance and brought a great challenge to public health (9).

Although the number of COVID-19 cases continues to grow worldwide, there are still uncertainties about its clinical characteristics, as well as risk factors associated with the development of disease or fatal outcome. Investigation of factors associated with survival is particularly problematic because there are no adequate guidelines for details of the clinical and virological course of the disease. Therefore, urgent

engagement of health services is needed to shed light on all the unknowns regarding COVID-19.

THE AIM OF THE PAPER

The aim of this study was to identify potential factors associated with survival in patients with COVID-19 to effectively predict the progression of the disease and allocate medical resources in a better way and to contribute to the identification of the basic epidemiological and clinical characteristics of this disease in laboratory-confirmed cases.

PATIENTS AND METHODS

Study design and participants

The study was designed as a case series. It included all patients hospitalized in Clinical Centre Kragujevac between March 10, 2020 (i.e. when the first patients were admitted), and June 15, 2020, due to COVID-19 which was confirmed by detection of SARS-CoV-2 in nasal and pharyngeal swab specimens with real-time reverse-transcriptase polymerase-chain-reaction (RT-PCR) assay. The inclusion criteria for the study were: confirmed infection by the RT-PCR test, hospitalization longer than 24 hours, signed informed consent for participation in the study, and that the patient was older than 18 years. The exclusion criterion was incomplete medical documentation. The study outcome was a survival event accompanied by the SARS-CoV-2 negativity and discharge of the patient from the hospital or fatal outcome. The study was approved by the Ethics Committee of Clinical Centre Kragujevac before its commencement.

Data collection

The data required for this examination were obtained by inspecting the patient's medical records or were extracted from electronic medical records. A trained team of physicians and research associates entered the obtained data on a standardized data collection form. The following variables were collected from the patient files: age of the patients, sex, date of admission to hospital or intensive care unit (ICU) and date of discharge, signs and symptoms of the disease experienced by the patients, co-morbidities, concomitant therapy, maximum values of haematological and biochemical tests during hospitalization, findings on chest X-ray or computed tomography (CT), acute respiratory distress syndrome (ARDS), adverse events as healthcare-associated infections (HAIs), applied therapy during the hospital stay including mechanical ventilation. Charlson Comorbidity Index was calculated for each patient (10).

Laboratory procedures

Isolation and identification of the causative agent of COVID-19 was performed in accordance with the Expert-Methodological Instruction (11) supported by the protocol established by the World Health Organization (12). According to the same guidelines, all samples were processed only



in reference laboratories and the obtained results were issued only as positive or negative for the presence of the virus.

Laboratory analyses were performed by standard methods in a hospital laboratory and included: complete blood count, serum biochemical tests (including renal and liver function, creatine kinase, lactate dehydrogenase, and electrolytes), myocardial enzymes and procalcitonin. The frequency of these examinations was determined by the treating physician or professional team.

Definitions

Lung examination included a mandatory X-ray or CT, and the severity of changes was defined based on the international guidelines for community-acquired pneumonia (13). ARDS was defined as acute-onset hypoxemia (the ratio of the partial pressure of arterial oxygen to the fraction of inspired oxygen [$\text{PaO}_2:\text{FiO}_2$] <300) with bilateral pulmonary opacities on chest imaging that were not fully explained by congestive heart failure or other forms of volume overload.

For the purposes of this study, a standard definition of HAIs by the Centers for Disease Control and Prevention (CDC), Atlanta, United States (14) was used, which means that the infection is not present and that there is no evidence of incubation at the time of admission to the hospital.

The criteria for discharge were the absence of fever for at least 3 days, clinical remission of respiratory symptoms, improvement in the lungs proved by X-ray, and two negative RT-PCR findings for virus SARS-CoV-2 obtained at least 24 h apart.

Statistical analysis

After coding and tabulation, the data were described statistically, using measures of central tendency (mean for normally distributed data and median for else) and dispersion (standard deviation for normally distributed data and interquartile range for else). The normality of the data distribution was checked by Kolmogorov-Smirnov's test. Categorical data were summarized by rates and percentages. Significance of differences in values of continuous variables among the study groups was tested by Student's T-test if normally distributed, and by Mann-Whitney U test if the distribution was not normal. Differences between the study groups in values of categorical variables were tested by Chi-square of Fisher's exact test, depending on whether the assumptions for the tests were satisfied. Variables with significant influence on the cure of patients with COVID-19 were identified by multivariate logistic regression, and strength of the influence was estimated by adjusted odds ratio. Quality of the regression model was estimated by Cox & Snell R square, Nagelkerke R square, and Hosmer and Lemeshow test. The results were considered significant if the probability of the null hypothesis was below or equal to 0.05. The Statistical Software for Social Sciences (SPSS) version 18 was used for calculations.

RESULTS

There were 234 patients with confirmed COVID-19 treated at the study hospital from March the 10th, to June the 15th, 2020. The average age of the patients was 57.2 ± 15.8 years. There were more male patients ($n=142$; 60.7%). Thirty-five patients died (15.0%) and 199 (85.0%) were discharged as completely cured and with the sustained virological response. Characteristics of the study patients are shown in Table 1, while the frequency of symptoms and signs of the disease is shown in Table 2. The study variables with significantly different values among the deceased and cured COVID-19 patients are shown in Table 3.

Multivariate logistic regression was performed to investigate influence of independent and confounding study variables on cure when it was adjusted for simultaneous influence of other variables. The final logistic regression model was construed using "enter" method, and it explained 49.8% (according to Cox & Snell R square) and 83.3% (according to Nagelkerke R square) of patient survival variability. Hosmer and Lemeshow test showed that observed cure rate was not significantly different from the expected cure rate according to our logistic regression model (Chi-square = 0.764; $p = 0.999$). The study variables with significant influence (expressed as odds ratio – OR) on cure of COVID-19 patients after adjustment for effects of other variables were: stay in an ICU (OR = 0.007; 95% confidence interval – CI 0.001 – 0.086; $p = 0.000$), previous hospitalization (OR = 7.802; 95% CI 1.198 – 50.924; $p = 0.032$), increased body temperature on admission (OR = 0.004; 95% CI 0.000 – 0.771; $p = 0.040$), higher score of the Charlson Comorbidity Index (OR = 0.428; 95% CI 0.235 – 0.780; $p = 0.006$), and increased values of C-reactive protein (CRP) serum level (OR = 0.978; 95% CI 0.966 – 0.990; $p = 0.000$). (Result is not shown).

DISCUSSION

The course of the COVID-19 pandemic so far has shown that the patients' treatment outcome largely depends on the resources available to the health system in a specific country. Therefore, clinicians need to be familiar with the factors associated with the treatment outcomes (cure or death) to early identify critical patients and to allocate rationally medical resources to them. Also, the good knowledge of these factors should enable the development of timely and customized treatment plan that could increase the efficiency of the health care system and reduce the possibility of fatal outcomes.

Our study showed relatively high intrahospital mortality (15.0%) of inpatients with COVID-19, which is directly associated with the fact that primarily patients with a more severe clinical presentation were admitted to the hospital. In accordance with the national Expert-Methodological Instruction (11), patients with the milder clinical presentation were referred to home treatment with adequate therapy. The cure rate was adversely affected by a stay in an ICU, increased body temperature on admission, the existence of comorbidities, and increased CRP levels. The only beneficial factor was



the previous hospitalization, while specific antiviral therapy, antibiotics, oxygen therapy, and mechanical ventilation did not affect the cure rate.

Increased body temperature is a sign which indicates that significant changes are taking place in the body. The fever as the only factor may not be the most significant criterion to determine the severity of illness, but diagnostic algorithms for COVID-19, which require the inclusion of temperature, can help in the prognosis of the disease. Therefore, an elevated temperature should be interpreted together with other signs and symptoms of the disease. Viral infection causes inflammation in the human body through the imbalance of T helper-1 and T helper-2 responses and an inflammatory storm by increasing the levels of inflammatory factors such as interleukin-4, interleukin-10, and interleukin-6 (15–17). This storm releases cytokines, causing systemic damage to the immune system associated with an increase in body temperature, which becomes an important sign of the onset of multiple organ failure that can ultimately lead to death (16–18). However, caution should be exercised in patients with a weak immune response when body temperature may be normal, even though the body is attacked by the virus.

In 60.4% of patients included in this study, there was at least one comorbidity, and the most common were hypertension (40.6%), coronary disease (17.5%), and diabetes mellitus (17.1%). However, the multivariate logistic regression model did not identify any comorbidity specifically as a factor with a negative impact on survival, which may, to some extent, be a consequence of the small sample size. Nevertheless, when the Charlson Comorbidity Index was calculated, it was shown that its higher values increase the risk of death outcome. This result has special importance for the clinicians because it indicates the need for calculating this index for each patient, especially if more comorbidities and older age are present. Already at the first examination of a patient, this index may warn the clinician that the patient is at risk for pneumonia with a potentially fatal outcome, which could then be prevented by undertaking adequate treatment measures. The prolonged persistence of comorbidity induces a state of the constant stress with a tendency to develop weak immunity (17). A long history of diabetes and hypertension will damage the vascular structure in the body and increase the likelihood that a critical illness will develop in the case of SARS-CoV-2 infection (17). Patients with chronic heart disease are more likely to have acute cardiovascular events and severe diseases due to their weakened heart function and poor immunity (17). Previous respiratory diseases, such as chronic obstructive pulmonary disease (COPD), weakens the pulmonary function by creating a tendency to develop ARDS in the case of SARS-CoV-2 infection (17). Recently published meta-analysis has shown that proportion of hypertension, diabetes, cardiovascular disease and respiratory disease was significantly higher in a group of patients in which a fatal outcome occurred (17).

During this study, a large number of laboratory parameters were monitored, however, apart from the increased value

of CRP, no other parameter was associated with unfavourable outcome. This can be partly explained by the fact that patients who had a more severe clinical presentation at the very beginning of the disease, usually accompanied by poor laboratory findings at the time of admission were hospitalized in our institution. Also, patients from other local hospitals were referred to our institution, as a tertiary care institution, in the phase of the clinical worsening of the disease or with already recorded poor laboratory parameters. Furthermore, we observed that our patients had renal dysfunction, as indicated by the increased levels of blood urea or creatinine at the time of admission and during hospitalization. Therefore, we think that an increased level of creatinine and urea nitrogen may also indicate poor prognosis. Numerous studies conducted so far (19,20) have indicated that some laboratory parameters are above reference range in COVID-19 patients and alanine aminotransferase (ALT), aspartate aminotransferase (AST), creatine kinase, lactate dehydrogenase, blood urea nitrogen, serum creatinine, C-reactive protein and procalcitonin particularly stand out among them, while leukocyte, lymphocyte, and platelet values decline. However, no laboratory parameter was brought directly in relation to the potentiation of the fatal outcome, which is dominantly in agreement with our results. Recently conducted study (21) has reported that values of D-dimer greater than $1 \mu\text{g/mL}$ on admission are associated with a higher chance of death for 18.42-fold (95% CI 2.64–128.55; $p = 0.0033$), while results of one recently published meta-analysis have indicated that those who died, compared to those who survived, differed on multiple laboratory parameters on admission including parameters such as elevated levels of CRP, D-dimer, cardiac troponin, interleukin-6 and ALT, as well as decreased levels of albumin (22).

Our study indicated an association of death outcome with an ICU stay, which is somewhat expected, given that patients with clinical exacerbations of the disease, such as severe pneumonia or ARDS, were transferred to ICU. Recent reports (23,24) suggest that approximately 14% to 30% of hospitalized patients with COVID-19 pneumonia requires admission to ICU, primarily for respiratory support in the setting of hypoxic respiratory failure. The rate of ARDS in COVID-19 varies by the cohort being reported, but seems to be high among hospitalised cohorts (25). A recent meta-analysis described an ARDS incidence of 14.8%, with case fatality rate of 4.3% (25). These critically ill patients are more often older men who have underlying comorbidities (23,24). The multicentre case series (26) states that the majority of patients with COVID-19 before their admission to the ICU had chronic illnesses, most commonly diabetes mellitus and chronic kidney disease which can all affect a poor treatment outcome.

It should also be emphasized that although HAIs were not found to be a significant factor that adversely affects the survival of COVID-19 patients, 8 patients (22.9%) who died had some HAI diagnosed compared to only 1 patient (0.5%) in the group of cured patients. It has been observed that the normal microbiological flora in patients who stay longer in the ICU is often replaced by strains from the hospital



environment, and it is known that ICUs are the area of high endemicity for many multi-resistant microorganisms. Colonization by such bacterial clones often precedes infection and occurs due to disruption of defence mechanisms caused by the underlying disease or the use of invasive medical procedures such as mechanical ventilation to which patients are often subjected. Furthermore, in cases of epidemics, there could be an inability to meet the standards regarding the nurse-patient relationship, which may lead to neglect of basic hygiene measures and further spread of hospital strains that cause infections, particularly with the application of numerous medical procedures required by such patients.

A significant result of this study is that COVID-19 patients who were previously hospitalized in another health care institution had 7.8-fold (95% CI 1.198 – 50.924; $p = 0.032$) increased chances of survival. Certainly, early identification and timely hospitalization of patients at risk of developing an unfavourable outcome, in addition to applied therapeutic measures, should contribute to cure and survival. Furthermore, this result should be interpreted through the fact that smaller hospitals were less burdened by patients which probably contributed to the timely observation of deterioration of patients' condition and provision of adequate medical care, which probably prevented many complications.

Our research had several limitations. First, this research was conducted in one health centre which may introduce bias due to certain local practices not present in other settings and the specific conditions of the hospital where the research was conducted. Second, the complete panel of laboratory analyses was not performed in some patients, so there were missing data regarding certain laboratory parameters for them. This could have had an impact on the results which included these variables. Third, this study included only hospitalized patients who basically had a more severe clinical presentation, while asymptomatic SARS-CoV-2 carriers and patients with a mild clinical presentation were treated at home and were not included in this study. Despite limitations, these data provide important information on the risk factors associated with death in patients with COVID-19 and provide the basis for some future research involving multiple factors in preventing its occurrence.

Table 1. Characteristics of the study patients.

Variable	Value (mean $\pm$ SD, median [IQR] if continuous, and rates if categorical)	Kolmogorov- Smirnov's test
Age (years)	57.2 $\pm$ 15.8, 58.8 [23.0]	$p = 0.025$
Sex (M/F)	142/92 (60.7% / 39.3%)	N/A
Duration of hospitalization (days)	15.2 $\pm$ 6.3, 15.0 [6.0]	$p = 0.000$
Patients treated at an ICU	55 (23.5%)	N/A
Length of stay in an ICU (n = 55)	9.9 $\pm$ 6.5, 8.0 [9.0]	$p = 0.007$
Previously hospitalized patients	92 (39.3%)	N/A
Length of previous hospitalization in days (n = 92)	3.8 $\pm$ 1.9, 3.0 [3.0]	$p = 0.000$
Patients with elevated body temperature	178 (76.1%)	N/A
Body temperature on admission in degrees Celsius (n = 178)	38.1 $\pm$ 2.9, 3.0 [3.0]	$p = 0.000$
Maximum white cell count ($\times 10^9/L$) (n = 200)	8.7 $\pm$ 4.6, 7.6 [5.4]	$p = 0.000$
Maximum lymphocyte count ($\times 10^9/L$) (n = 200)	1.2 $\pm$ 1.2, 0.9 [0.7]	$p = 0.000$
Maximum platelet count ($\times 10^9/L$) (n = 200)	225.7 $\pm$ 89.9, 215.5 [108.5]	$p = 0.018$
Maximum haemoglobin level (g/L) (n = 200)	124.4 $\pm$ 20.0, 126.5 [25.0]	$p = 0.200$
Maximum C-reactive protein level in serum (mg/L) (n = 200)	108.2 $\pm$ 124.2, 68.2 [156.9]	$p = 0.000$
Maximum LDH level in serum (U/L) (n = 200)	580.1 $\pm$ 251.4, 529.5 [306.5]	$p = 0.000$
Maximum creatinine level in serum (microM/L) (n = 211)	167.5 $\pm$ 263.9, 87.0 [38.0]	$p = 0.000$
Maximum D-dimer level in serum (mcg/L) (n = 208)	8.7 $\pm$ 47.9, 0.8 [1.5]	$p = 0.000$
Maximum procalcitonin level in serum (ng/ml) (n = 159)	0.91 $\pm$ 3.29, 0.09 [0.27]	$p = 0.000$
Maximum proBNP level in serum (pg/ml) (n = 143)	2661.7 $\pm$ 6599.5, 359.0 [1478.0]	$p = 0.000$



Variable	Value (mean $\pm$ SD, median [IQR] if continuous, and rates if categorical)	Kolmogorov- Smirnov's test
Maximum troponin I level in serum (ng/ml) (n = 125)	0.08 $\pm$ 0.28, 0.01 [0.01]	p = 0.000
Maximum serum level of glucose (mM/L) (n = 215)	7.8 $\pm$ 7.8, 6.1 [2.5]	p = 0.000
Maximum serum level of urea (mM/L) (n = 223)	12.2 $\pm$ 28.8, 6.4 [6.2]	p = 0.000
Maximum creatine kinase level in serum (U/L) (n = 214)	202.2 $\pm$ 457.9, 101.5 [99.5]	p = 0.000
Maximum creatine kinase muscle brain (CK-MB) level in serum (U/L) (n = 176)	15.5 $\pm$ 13.9, 12.0 [6.0]	p = 0.000
Charlson Comorbidity Index (n = 234)	2.2 $\pm$ 1.9, 2.0 [4.0]	p = 0.000
Hypertension	95 (40.6%)	N/A
Coronary disease	41 (17.5%)	N/A
Diabetes mellitus	40 (17.1%)	N/A
COPD	31 (13.2%)	N/A
Chronic renal failure	18 (7.7%)	N/A
Myocardial infarction	4 (1.7%)	N/A
Cerebrovascular disease	9 (3.8%)	N/A
Cancer	7 (3.0%)	N/A
Hypothyroidism	3 (1.3%)	N/A
Bronchial asthma	3 (1.3%)	N/A
Leukaemia	2 (0.9%)	N/A
Chronic sinusitis	1 (0.4%)	N/A
Parkinsonism	1 (0.4%)	N/A

Abbreviations: COPD – chronic obstructive pulmonary disease; F – female; ICU – intensive care unit; IQR – interquartile range; LDH – lactate dehydrogenase; M – male; N/A – not applicable; SD – standard deviation.

Table 2. Frequency of signs and symptoms in patients with COVID-19.

Sing or symptom	Frequency n (%)
Cough	135 (57.7%)
Weakness	74 (31.6%)
Dyspnoea	50 (21.4%)
Throat pain	33 (14.1%)
Muscle pain	30 (12.8%)
Diarrhoea	30 (12.8%)
Nausea	26 (11.1%)
Pain in the joints	24 (10.3%)
Headache	20 (8.5%)
Expectoration	17 (7.3%)
Anosmia	14 (6.0%)
Shivering	13 (5.6%)
Vomiting	12 (5.1%)
Nasal secretion	10 (4.3%)
Confusion	3 (1.3%)
Conjunctivitis	1 (0.4%)
Fatigue	1 (0.4%)
Anxiety	1 (0.4%)

Table 3. The study variables that were significantly different among the deceased and cured patients (univariate analysis).

Variable	Deceased patients (n = 35), median [IQR]	Cured patients (n = 199), median [IQR]	Statistical test value and probability of null hy- pothesis
Age (years)	69.0 [23.0]	56.0 [23.0]	Mann-Whitney U = 2,203.00; p = 0.001
Length of hospitalization (days)	12.0 [11.0]	15.0 [6.0]	Mann-Whitney U = 4,322.00; p = 0.023
Body temperature on admission (de- grees Celsius)	38.6 [1.0]	38.0 [0.6]	Mann-Whitney U = 1,564.00; p = 0.001
Maximum white cell count (x 10 ⁹ /L)	13.8 [7.5]	6.9 [4.9]	Mann-Whitney U = 938.50; p = 0.000
Maximum lymphocyte count (x 10 ⁹ /L)	0.6 [0.6]	1.0 [0.8]	Mann-Whitney U = 3,040.0; p = 0.002
Maximum platelet count (x 10 ⁹ /L)	162.0 [117.5]	222.0 [106.0]	Mann-Whitney U = 4,712.00; p = 0.000
Maximum haemoglobin level (g/L)	104.0 [33.5]	128.0 [25.0]	Mann-Whitney U = 5,281.50; p = 0.000
Maximum C-reactive protein level in serum (mg/L)	278.0 [139.0]	49.0 [104.4]	Mann-Whitney U = 547.50; p = 0.000
Maximum LDH level in serum (U/L)	826.5 [353.8]	501.5 [280.0]	Mann-Whitney U = 509.50; p = 0.000
Maximum creatinine level in serum (microM/L)	125.0 [322.0]	84.0 [31.0]	Mann-Whitney U = 1,745.00; p = 0.000
Maximum procalcitonin level in se- rum (ng/ml)	1.73 [3.95]	0.07 [0.15]	Mann-Whitney U = 433.50; p = 0.000
Maximum troponin I level in serum (ng/ml)	0.03 [0.1]	0.01 [0.01]	Mann-Whitney U = 433.50; p = 0.000
Maximum serum level of urea (mM/L)	14.6 [16.2]	5.8 [4.4]	Mann-Whitney U = 1,100.0; p = 0.000
Maximum creatine kinase level in se- rum (U/L)	158.0 [164.0]	93.0 [87.0]	Mann-Whitney U = 1,871.50; p = 0.000
Stay in an ICU	33 (94.3%)	55 (23.5%)	Chi-Square = 114.68 p = 0.000
Increased body temperature at admis- sion	34 (97.1%)	144 (72.4%)	Chi-Square = 10.04 p = 0.002
Nausea	8 (22.9%)	18 (9%)	Chi-Square = 5.75 p = 0.016
Vomiting	5 (14.3%)	7 (3.5%)	Fisher's exact test, p = 0.020
Diabetes mellitus	11 (31.4%)	29 (14.6%)	Chi-Square = 5.97 p = 0.015
COPD	11 (31.4%)	20 (10.1%)	Chi-Square = 11.84 p = 0.001
Chest X-ray findings • Normal • unilateral opacities • bilateral opacities • ground-glass opacities • crazy paving appear- ance	0 (0%) 7 (20.0%) 24 (68.6%) 3 (8.6%) 1 (2.9%)	55 (27.6%) 52 (26.1%) 63 (31.7%) 13 (6.5%) 15 (7.5%)	Chi-Square = 22.34 p = 0.000
X-ray signs of pneumonia	35 (100%)	137 (68.8%)	Chi-Square = 14.84 p = 0.000
ARDS	30 (85.7%)	2 (1.0%)	Chi-Square = 180.93



Variable	Deceased patients (n = 35), median [IQR]	Cured patients (n = 199), median [IQR]	Statistical test value and probability of null hy- pothesis
			p = 0.000
Sepsis	6 (17.1%)	1 (0.5%)	Chi-Square = 28.40 p = 0.000
Mechanical ventilation	33 (94.3%)	10 (5.0%)	Chi-Square = 158.11 p = 0.000
Administration of antibiotics	35 (100%)	171 (85.9%)	Chi-Square = 5.59 p = 0.018
Nosocomial infection	8 (22.9%)	1 (0.5%)	Chi-Square = 40.22 p = 0.000

Abbreviations: ARDS - Acute Respiratory Distress Syndrome; COPD – chronic obstructive pulmonary disease; ICU – intensive care unit; IQR – interquartile range; LDH – lactate dehydrogenase.

CONCLUSION

In conclusion, early diagnosis and timely treatment are crucial in reducing mortality in COVID-19 patients. The results of this study could help clinicians to identify patients with poor prognosis at an early stage of disease by being aware of some of the alarming clinical characteristics presented by the patients. Special attention should be paid to patients who have high body temperature at admission, presence of multiple comorbidities, high values of CRP in the serum, and patients who stay in an ICU, considering that they could have an increased risk for fatal outcome.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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