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ORIGINAL RESEARCH

Mortality Due to Covid-19 in Hospitalized Patients: A Prediction Model Based on Different Risk Factors

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Video abstract

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Purpose: Since 2020, COVID-19 severely affected the world population, generating numerous deaths and a great socioeconomic impact that affected the healthcare system. This investigation aimed to analyze a prediction model for COVID-19 mortality on the basis of different risk factors.

Patients and Methods: Retrospective, cross-sectional study in a sample of 2000 hospitalized patients. Biological and clinical factors (signs and symptoms), laboratory/diagnostic results and comorbidities were taken into account. The SPSS version 29 statistical package was used to process the information, performing a bivariate and multivariate analysis with binary logistic regression using the intro methods.

Results: Most of the deceased were male, older than 60 years, blood type O positive, hypertensive, type 2 diabetic, obese. The most common symptoms were fever, malaise, shortness of breath and fatigue, the most common tomography findings were bilateral ground glass with BiRad 5 scale in more seriously impaired patients.

Conclusion: An adequate model was obtained with a 76% prognostic rate. The variables included in the predictive model for COVID-19 mortality were age, fever, productive cough, sore throat, fatigue, shortness of breath, unilateral consolidation on CT scan, hemoglobin level, leucocyte count, lymphocytes, platelets, urea, and ferritin.

Keywords: SARS CoV-2, COVID-19, risk factors, signs and symptoms, mortality

Introduction

The global population has been profoundly impacted by the ongoing pandemic, with widespread fatalities and significant socioeconomic consequences. In 2021, the number of deaths related to the virus worldwide totaled approximately 3.8 million. However, this figure fell substantially to 1.2 million in 2022. By the first quarter of 2023, global mortality from the virus had decreased dramatically, reaching approximately 17 times fewer deaths than the previous year, indicating a possible end to the pandemic. Consequently, on 5 May 2023, the World Health Organization (WHO) announced COVID-19 no longer constituted a global health emergency.[1]

In Peru, since the onset of the COVID-19 pandemic, a total of 4,523,877 cases have been diagnosed, resulting in 221,578 deaths, corresponding to a case fatality rate of 4.90%. In the Department of La Libertad, 11,100 deaths have been reported, with a case fatality rate of 6.08% This department has a predominantly urban population but with large rural areas, which is why there were deficiencies in access to medical care, availability of oxygen and hospital capacity.[2]

In Lima, the capital city with a population of 10.4 million, studies have shown that the risk of hospitalization due to COVID-19 significantly increases among individuals aged 70 and older, with a higher prevalence observed in men.[3] Furthermore, the likelihood of hospitalization in men is estimated to be approximately twice that of women.[4]

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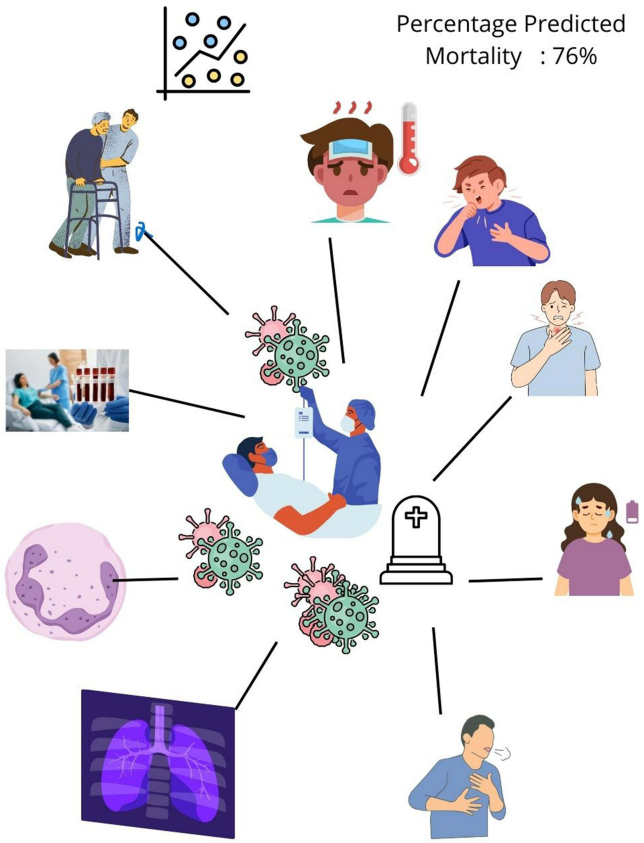
Graphical Abstract



Additionally, research indicates that the majority of hospitalized COVID-19 patients have comorbidities such as hypertension, obesity, chronic lung disease, and type 2 diabetes mellitus. These underlying conditions have been linked with a higher risk of mortality from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.[5,6]

Laboratory data analyses have been used to examine the correlation between various factors and mortality from the novel coronavirus (SARS-CoV-2), yielding varied findings. For instance, a study conducted in the Peruvian Amazon region of Ucayali identified high leukocyte and neutrophil counts, as well as high D-dimer concentrations, as risk factors for increased mortality, whereas higher lymphocyte levels were associated with lower mortality.[7]

In contrast, research on older adults in Lima indicated that elevated levels of D-dimer, C-reactive protein (CRP), total bilirubin, albumin and alanine aminotransferase (ALT) were associated with a higher risk of mortality. Lower lymphocyte counts were also found to be a contributing factor.[8]

Since the emergence of the COVID-19 pandemic in 2019, extensive research has explored various aspects of the disease. Findings indicate that approximately 75% of patients remained asymptomatic, while 4.4% experienced severe COVID-19.[9] Reported symptoms include cough, fever, and shortness of breath,[9,10] along with myalgia, headache, anosmia, dysgeusia, sore throat, and chest pain. Additionally, computed tomography (CT) scans revealed severe pulmonary involvement in 7.3% of cases, whereas 3.6% exhibited mild to moderate lung damage,[9,11] and some patients presented with pneumonia of previously unidentified etiology.[12] Among the biological factors linked to COVID-19 mortality, advanced age has been identified as a significant risk factor, with a reported mean age of 60.2 years (±15.6).[9,11,13–15]

Studies across multiple countries have consistently shown a higher mortality rate among men compared to women,[12] with males facing an approximately twofold increased risk of death.[16,17] Furthermore, individuals of Asian, mixed ethnicity,[17] and

African descent[18] have been associated with a higher mortality risk. Another biological factor correlated with increased COVID-19 mortality is blood type A.[19]

Several clinical factors have been identified as contributors to increased COVID-19 mortality. These include an elevated respiratory rate (OR 1.5), moderate (OR 1.7) or severe (OR 2.9) pneumonia,[15] a history of cardiomyopathy (OR 3.33), positive findings on initial chest imaging (OR 2.24), and acute kidney injury (OR 3.33).[13,14] Additionally, patients with diabetes, lymphopenia, and elevated procalcitonin levels have also been linked to a higher risk of death.[16] In Brasilia, research has found a significant association between patient mortality and low hemoglobin (Hb) levels ($p<0.001$), erythroblastosis (OR 8.3), lymphopenia, thrombocytopenia with platelet counts below 50,000/mm³ (OR 5.2), elevated D-dimer levels (OR 7.5), the need for transfusion (OR 3.7), and increased ferritin concentrations ($p=0.0002$).[20]

Other biomarkers associated with mortality include elevated aspartate aminotransferase, lactate dehydrogenase, procalcitonin, creatine kinase, and C-reactive protein. Additionally, the need for oxygen therapy within the first 48 hours, noninvasive ventilation, and mechanical ventilation were significantly linked to increased mortality risk. Treatment with interferon-beta was also reported as a contributing factor (OR 1.5).[15] Furthermore, in some patients, mortality was associated with the malignancy of the disease, as well as the presence of prior surgery or trauma.[9] In Spain, a notable increase in mortality was observed among COVID-19 patients diagnosed with hip fractures.[21]

Individuals with pre-existing comorbidities have been observed to be at greater risk of developing complications and experiencing higher mortality rates due to COVID-19. Among the most frequently reported comorbid conditions associated with increased mortality risk are obesity (OR: 5.272),[22] chronic hypertension (OR: 2.1),[23] moderate to severe liver disease,[17] diabetes mellitus,[10] cardiovascular disease, human immunodeficiency virus (HIV) infection,[9] cancer, chronic obstructive pulmonary disease (COPD),[14] and ischemic heart disease.[24]

Additional factors contributing to COVID-19-related mortality include the absence of medical treatment during the symptomatic phase (OR: 5.27), limited hospital bed availability (OR: 1.16),[11] lack of vasopressor support, and insufficient oxygen therapy equipment. The patterns of COVID-19 morbidity and mortality are largely influenced by population density, demographic characteristics, underlying health conditions, viral transmission dynamics, the nature of the virus itself, and environmental factors.[12]

COVID-19, initially detected in December 2019 in Wuhan, Hubei Province, China, was officially declared a pandemic in March 2020. This designation followed a rapid and exponential increase in morbidity and mortality, initially across China and subsequently worldwide.[25,26] Our country reported the first case in epidemiological week 10 of 2020.[27] This phenomenon contributed to the evaluation of cases, their positive and negative evolution, the symptomatology of COVID-19 and the factors contributing to its presence.[28]

It is a respiratory disease characterized by severe respiratory syndrome, caused by the betacoronavirus SARS-CoV-2. Typically, symptoms appear between five and 15 days after exposure and may include fever, headache, cough, sore throat, sneezing and diarrhea.

If it evolves to pneumonia, it also manifests with dyspnea and bilateral infiltrates on auscultation. Patients with comorbidities may develop more severe respiratory clinical picture in addition to cardiac failure, encephalopathies or bacterial or viral co-infections. Symptomatology and partial, total recovery or death of the patient, which depends on many factors.[29,30]

In this regard, it was pointed out that most patients infected with an acute COVID-19 process recovered their initial health. However, between 10% and 20% did not recover completely, manifesting long-term effects in various body systems,[31] generating alarming morbidity and mortality statistics, despite the extreme sanitary measures adopted since the beginning of the pandemic.[32]

In 2021, it was already reported that there are differences between countries in the Americas in relation to socioeconomic, cultural and clinical factors that determine the level of impact of COVID-19. Currently, these differences persist, causing each country, according to its particularities, to take various health measures to avoid outbreaks of the pandemic.[33] In this regard, it is specified that the identification of these factors, mainly in at-risk populations, contributes to propose strategies for prevention and timely treatment.[30] Likewise, it has been indicated that the health status of the population determines the behavior of covid-19,[34,35] stating that regardless of the patients' age, the presence of chronic neurological, renal, hepatic and cancer diseases, they would have a high risk of dying from this pathology,[35] making relevant the importance of considering comorbidities in patients affected with COVID-19, since they are significantly associated with the patient's mortality.[30]

Most studies on COVID-19 prediction models have focused primarily on laboratory parameters and symptoms. In the present study, clinical imaging results were considered in the predictive model, which contributes to timely treatment prescriptions, both during and after the illness.

The general objective was to determine a predictive model for factors associated with mortality due to COVID 19 in hospitalized patients in La Libertad.

Materials and Methods

Type of Study and Research Design

Descriptive, basic study, quantitative approach, retrospective, cross-sectional correlational design.[36]

Study Population

The population consisted of 6328 medical records of patients in the La Libertad Region with COVID-19 treated in COVID-19 ESSALUD Trujillo hospitals during the pandemic period, that is, in the year 2020. The sample included 2000 randomly selected patients, taking into account an error of 1.18% and 95% reliability, which makes it a representative and adequate sample.[37]

Figure 1 shows patient selection process flowchart. Of the 6,328 hospitalized patients diagnosed with COVID-19, 3,372 were excluded due to lack of diagnostic tests and 956 due to incomplete data, leaving a final sample of 2,000 patients.

Although a predetermined sample size calculation based on power analysis for logistic regression was not performed, the total number of cases and the high proportion of events (53% mortality) met the methodological criterion of at least 10 events per predictor included in the model (84 predictors). This indicates adequate statistical power to detect associations of moderate or strong magnitude (eg, OR>2). However, it is recognized that for low-prevalence variables such as diabetes mellitus, the

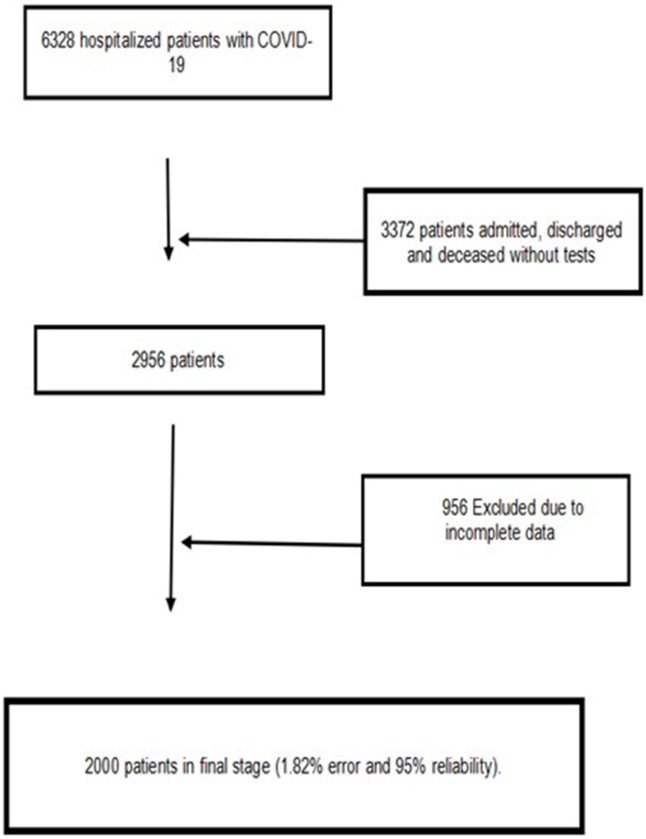


Figure 1 Patient selection process flowchart.

power to identify small or marginal associations could have been insufficient, especially in the case of p-values close to the significance threshold.[37]

The period considered is from March to December 2020, which included two waves, the first and second. The first two were taken into account to emphasize the characteristics prior to vaccination. As this is a retrospective study, the cutoff points were taken into account according to the peaks of the highest incidence of the disease.

For the collection of information, a documentary analysis was carried out. The patients' medical records were reviewed using the data collection form as an instrument, which included the following factors according to their epidemiological nature:

Biological factors: age, sex and blood group.

Clinical Factors (Signs and Symptoms)

Asymptomatic, fever, malaise, dry cough, productive cough, pleuritic pain, hemoptysis, sore throat, rhinorrhea, dysgeusia, anosmia, muscle pain, fatigue, shortness of breath, diarrhea, headache, pneumothorax, liver failure, other symptoms.

Diagnostic Imaging

Ground-glass tomography, pulmonary involvement scale by tomography.

Laboratory results: hemoglobin, hematocrit, leukocytes, abastonates, lymphocytes, neutrophils, platelets, creatinine, urea, fibrinogen, ferritin, D-dimer.

Comorbidities

Obesity, asthma, diabetes, arterial hypertension, chronic kidney disease according to stages, acute injury, ischemic disease, absence of viral load, history of TB, HIV, hepatitis, fatty liver, cirrhosis, cancer, chronic lung disease, third trimester of pregnancy, natural childbirth, hyperglycemia, other comorbidities and the number of comorbidities.

Statistical Analysis

The data compiled into an Excel database and analyzed using SPSS version 29. Descriptive statistics were used to summarize the information in statistical measures and double entry tables. Likewise, to select the biological, clinical factors, laboratory results, diagnosis, mortality risk comorbidities in hospitalized patients with COVID-19, multivariate analysis was conducted using binary logistic regression.[38]

Prior to multivariate analysis, data quality control was performed, eliminating records with critical or inconsistent missing data.

Regarding the assumptions of binary logistic regression, multicollinearity was assessed by calculating the Variance Inflation Factor (VIF), considering values < 5 as indicative of the absence of significant collinearity between predictors.

Linearity analysis was not performed on the log-odds ratio, which is recognized as a limitation of the multivariate model applied.

Ethical Considerations

Since it is a retrospective study, informed consent from the patient was not required. Authorization was obtained from the La Libertad Health Care Network, which allowed access to patient information through the medical history, the study being part of a project approved with certificate No. 88 of November 14, 2023. Furthermore, ethical approval was obtained from the ethics committee of the School of Medicine at César Vallejo University (Opinion 363-CEI-EPM-UCV-2023). The study adhered to the principles outlined in the Declaration of Helsinki, including anonymity, respect, beneficence and justice.[39]

Results

Table 1 shows that most of the persons who died from COVID 19 were males with O-positive blood type. In the bivariate analysis, no significant association was found among the variables analyzed. The average age of persons hospitalized with COVID 19 was higher in those who died and differed from those who did not die.

In the analysis of the associated comorbidities presented in Table 2, we can see that most of the deceased persons had hypertension, diabetes, obesity and other comorbidities. We observed an association between the variables hypertension,

Table 1 Biological Factors According to COVID-19 Mortality

Biological Factors		MORTALITY				Total	%	sig.
		NO	%	YES	%			
Sex	Female	300	15.0	313	15.7	613	30.7	0.17*
	Male	633	31.7	754	37.7	1387	69.4	
A positive	No	914	45.7	1047	52.4	1961	98.1	0.79*
	Yes	19	1.0	20	1.0	39	2.0	
B positive	No	930	46.5	1061	53.1	1991	99.6	0.42*
	Yes	3	0.2	6	0.3	9	0.5	
0 positive	No	662	33.1	764	38.2	1426	71.3	0.75*
	Yes	271	13.6	303	15.2	574	28.7	
0 negative	No	932	46.6	1066	53.3	1998	99.9	0.92*
	Yes	1	0.1	1	0.1	2	0.%	
AB positive	No	931	46.6	1066	53.3	1997	99.9	0.49*
	Yes	2	0.1	1	0.1	3	0.2	
Total		933	46.7	1067	53.4	2000	100	
Age (X ± s) (Me± RI)		57.51±13.56 58±19		65.39 ±13.01 66±18		61.71±13.84 62±8		0.00**

Notes: *Chi-square was used, **Mann Whitney U was used.

Table 2 Distribution of Covid 19 Mortality According to Comorbidities in Hospitalized Patients, La Libertad, Peru

Comorbidity		MORTALITY				Total	%	sig.
		NO	%	YES	%			
Obesity	No	727	36.4	835	41.8	1562	78.1	0.86*
	Yes	206	10.3	232	11.6	438	21.9	
Asthma	No	915	45.8	1054	52.7	1969	98.5	0.20*
	Yes	18	0.9	13	0.7	31	1.6	
Diabetes Mellitus type 2	No	757	37.9	830	41.5	1587	79.4	0.07*
	Yes	176	8.8	237	11.9	413	20.7	
Hypertension	No	577	28.9	567	28.4	1144	57.2	0.00*
	Yes	356	17.8	500	25.0	856	42.8	
Stage 5 chronic kidney disease	No	925	46.3	1032	51.6	1957	97.9	0.00*
	Yes	8	0.4	35	1.8	43	2.2	
Stage 4 chronic kidney disease	No	929	46.5	1063	53.2	1992	99.6	0.85*
	Yes	4	0.2	4	0.2	8	0.4	

(*Continued*)

Table 2 (Continued).

Comorbidity		MORTALITY				Total	%	sig.
		NO	%	YES	%			
Stage 3 chronic kidney disease	No	928	46.4	1053	52.7	1981	99.1	0.07*
	Yes	5	0.3	14	0.7	19	1.0	
Stage 2 chronic kidney disease	No	927	46.4	1064	53.2	1991	99.6	0.23*
	Yes	6	0.3	3	0.2	9	0.5	
Stage 1 chronic kidney disease	No	932	46.6	1066	53.3	1998	99.9	0.92*
	Yes	1	0.1	1	0.1	2	0.1	
Acute lesion	No	931	46.6	1056	52.8	1987	99.4	0.02*
	Yes	2	0.1	11	0.6	13	0.7	
Ischemic disease	No	927	46.4	1052	52.6	1979	99.0	0.09*
	Yes	6	0.3	15	0.8	21	1.1	
Absence of viral load	No	933	46.7	1065	53.3	1998	99.9	0.2*
	Yes	0	0.0	2	0.1	2	0.1	
TBC History	No	931	46.6	1063	53.2	1994	99.7	0.51*
	Yes	2	0.1	4	0.2	6	0.3	
HIV	No	933	46.7	1065	53.3	1998	99.9	0.54*
	Yes	0	0.0	2	0.1	2	0.1	
Hepatitis C	No	933	46.7	1066	53.3	1999	100.0	1*
	Yes	0	0.0	1	0.1	1	0.1	
Hepatitis B	No	932	46.6	1066	53.3	1998	99.9	0.92*
	Yes	1	0.1	1	0.1	2	0.1	
Fatty liver	No	932	46.6	1067	53.4	1999	100.0	0.29*
	Yes	933	0.1	0	0.0	1	0.1	
Non-alcoholic cirrhosis	No	933	46.7	1057	52.9	1990	99.5	0.00*
	Yes	0	0.0	10	0.5	10	0.5	
Decompensation due to cirrhosis	No	933	46.7	1065	53.3	1998	99.9	0.54*
	Yes	0	0.0	2	0.1	2	0.1	
Carcinoma	No	933	46.7	1066	53.3	1999	100.0	1*
	Yes	0	0.0	1	0.1	1	0.1	
Chronic lung disease	No	931	46.6	1057	52.9	1988	99.4	0.07*
	Yes	2	0.1	10	0.5	12	0.6	
Hyperglycemia	No	898	44.9	993	49.7	1891	94.6	0.02*
	Yes	35	1.8	74	3.7	109	5.5	

(*Continued*)

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Table 2 (Continued).

Comorbidity		MORTALITY				Total	%	sig.
		NO	%	YES	%			
Other comorbidities	No	683	34.2	715	35.8	1398	69.9	0.00*
	Yes	250	12.5	352	17.6	602	30.1	
Total		933	46.7	1067	53.4	2000	100	
No. of comorbidities (X ± s) (Me± RI)		1.14±1.21 1±2		1.43±1.34 1±2		1.30±1.29 1±2		0.00**

Notes: *Chi-square was used, **Mann Whitney U was used.

Stage 5 chronic kidney disease, acute injury, non-alcoholic cirrhosis, hyperglycemia and other comorbidities with mortality due to COVID 19, and inferred that the presence of these comorbidities would increase mortality due to COVID 19. The number of comorbidities and the total number of symptoms differed and their average was higher in those who died.

In Table 3 we analyzed the signs and symptoms, noting that most of the people who died presented signs and symptoms such as fever, malaise, shortness of breath and fatigue. In the bivariate analysis, fever, malaise, dry cough, productive cough, pleuritic pain, hemoptysis, sore throat, rhinorrhea, digestion, anosmia, fatigue, shortness of breath and diarrhea are associated with mortality due to COVID 19, which would indicate that their presence increases the risk of mortality.

Table 3 Signs and Symptoms According to COVID-19 Mortality in Hospitalized Patients in La Libertad - Peru

Signs and Symptoms		MORTALITY				Total	%	sig.
		NO	%	YES	%			
Asymptomatic	No	931	46.6	1059	53.0	1990	99.5	0.09*
	Yes	2	0.1	8	0.4	10	0.5	
Fever	No	123	6.2	77	3.9	200	10.0	0.00*
	Yes	810	40.5	990	49.5	1800	90.0	
Malaise	No	83	4.2	137	6.9	220	11.0	0.00*
	Yes	850	42.5	930	46.5	1780	89.0	
Dry cough	No	357	17.9	670	33.5	1027	51.4	0.00*
	Yes	576	28.8	397	19.9	973	48.7	
Productive cough	No	699	35.0	486	24.3	1185	59.3	0.00*
	Yes	234	11.7	581	29.1	815	40.8	
Pleuritic pain	No	924	46.2	1043	52.2	1967	98.4	0.02*
	Yes	9	0.5	24	1.2	33	1.7	
Hemoptysis	No	927	46.4	1040	52.0	1967	98.4	0.00*
	Yes	6	0.3	27	1.4	33	1.7	

(*Continued*)

Table 3 (Continued).

Signs and Symptoms		MORTALITY				Total	%	sig.
		NO	%	YES	%			
Sore throat	No	288	14.4	382	19.1	670	33.5	0.02*
	Yes	645	32.3	685	34.3	1330	66.5	
Rhinorrhea	No	469	23.5	576	28.8	1045	52.3	0.09*
	Yes	464	23.2	491	24.6	955	47.8	
Dysgeusia	No	590	29.5	743	37.2	1333	66.7	0.00*
	Yes	343	17.2	324	16.2	667	33.4	
Anosmia	No	553	27.7	710	35.5	1263	63.2	0.00*
	Yes	380	19.0	357	17.9	737	36.9	
Muscle pain	No	130	6.5	165	8.3	295	14.8	0.34*
	Yes	803	40.2	902	45.1	1705	85.3	
Fatigue	No	209	10.5	102	5.1	311	15.6	0.00*
	Yes	724	36.2	965	48.3	1689	84.5	
Shortness of breath	No	645	32.3	341	17.1	986	49.3	0.00*
	Yes	288	14.4	726	36.3	1014	50.7	
Diarrhea	No	795	39.8	846	42.3	1641	82.1	0.00*
	Yes	138	6.9	221	11.1	359	18.0	
Headache	No	163	8.2	217	10.9	380	19.0	0.10*
	Yes	770	38.5	850	42.5	1620	81.0	
Pneumothorax	No	926	46.3	1051	52.6	1977	98.9	0.12*
	Yes	7	0.4	16	0.8	23	1.2	
Hepatic insufficiency	No	931	46.6	1062	53.1	1993	99.7	0.34*
	Yes	2	0.1	5	0.3	7	0.4	
Other symptoms	No	925	46.3	1047	52.4	1972	98.6	0.05*
	Yes	8	0.4	20	1.0	28	1.4	
Total		933	46.7	1067	53.4	2000	100	

Note: *Chi-square was used.

According to Table 4, where laboratory/diagnostic results are presented, the majority of the deceased persons had Level 2 ground-glass CT scan of the lung and level 5 pulmonary involvement by tomography. Hematocrit, hemoglobin, lymphocytes, platelets have lower average values in the deceased, differing from the non-deceased; leukocytes, abastonates, neutrophils, creatinine, urea and ferritin have higher average values in the deceased, differing from the non-deceased.

In the multivariate analysis shown in Table 5, we observed that the variables age, fever, productive cough, sore throat, fatigue, shortness of breath, unilateral consolidation tomography, hemoglobin level, leukocyte count, abastonates, lymphocytes, platelets, urea, and ferritin are those that entered the predictive model for mortality due to COVID 19.

Table 4 Laboratory/Diagnostic Results According to Mortality by COVID-19 in Hospitalized Patients in La Libertad - Peru

Laboratory/Diagnostic Results		MORTALITY				Total	%	Sig.
		NO	%	YES	%			
Level 1 ground-glass CT scan of the lung	No	909	45.5	1047	52.4	1956	97.8	0.29*
	Yes	24	1.2	20	1.0	44	2.2	
Level 2 ground-glass CT scan of the lung	No	619	31.0	485	24.3	1104	55.2	0.00*
	Yes	314	15.7	582	29.1	896	44.8	
Unilateral consolidated tomography	No	907	45.4	1057	52.9	1964	98.2	0.00*
	Yes	26	1.3	10	0.5	36	1.8	
Bilateral consolidation tomography	No	552	27.6	732	36.6	1284	64.2	0.00*
	Yes	381	19.1	335	16.8	716	35.8	
CoRad 5	No	237	11.9	180	9.0	417	20.9	0.00*
	Yes	696	34.8	887	44.4	1583	79.2	
CoRad 4	No	911	45.6	1043	52.2	1954	97.7	0.87*
	Yes	22	1.1	24	1.2	46	2.3	
CoRad 3	No	912	45.6	1042	52.1	1954	97.7	0.89*
	Yes	21	1.1	25	1.3	46	2.3	
CoRad 2	No	933	46.7	1066	53.3	1999	100.0	1*
	Yes	0	0.0	1	0.1	1	0.1	
CoRad 1	No	931	46.6	1067	53.4	1998	99.9	0.42*
	Yes	2	0.1	0	0.0	2	0.1	
Hematocrit (X ± s) (Me± RI)		39.26±6.10 40.10±7.5		37.39±10.18 39.1±8.5		38.26±8.57 39.6±8.10		0.00**
Hemoglobin (X ± s) (Me± RI)		13.51±1.96 13.70±2.20		12.78±3.51 13.20±2.70		13.12±2.92 13.14±2.50		0.00**
Leucocytes (X ± s) (Me± RI)		10,650.91±7459.16 9450±7135		13,752.63± 8301.97 13,220± 9810		12,305.67± 8067.87 11,175± 9174.75		0.00**
Abastonated (X ± s) (Me± RI)		0.22±0.73 0±0		0.41± 1.03 0± 0		0.32± 0.91 0.00± 0.00		0.00**
Lymphocytes (X ± s) (Me± RI)		1.36±1.60 1.12±0.97		0.96± 1.43 0.74± 0.63		1.15±1.52 0.89± 0.81		0.00**
Neutrophils (X ± s) (Me± RI)		9143.34±8933.04 7440±7430		12,388.57±9149.89 11,495±10,030		11,631.23± 19,156.60 9090± 9695		0.00**
Platelets (X ± s) (Me± RI)		319.56± 117.34 310± 155.50		277.41± 129.48 271± 150		297.0760+126.36 289+151.75		0.00**
Creatinine (X ± s) (Me± RI)		0.89± 0.96 0.78± 0.36		1.25± 1.68 0.83± 0.56		1.3064±6.26 0.8±0.45		0.00**

(*Continued*)

Table 4 (Continued).

Laboratory/Diagnostic Results		MORTALITY				Total	%	Sig.
		NO	%	YES	%			
Urea (X ± s) (Me± RI)		32.18±28.45 31±23		52.37± 57.62 40± 36		42.94±47.42 35±28		0.00**
Fibrinogen (X ± s) (Me± RI)		60.17±168.05 0±0		53.94± 219.26 0± 0		56.84+197.011 0+0		0.34**
Ferritin (X ± s) (M± RI)		425.86±796.17 0±676.05		802.12± 188.05 0± 1074		626.5947± 1492 0± 835.83		0.00**
Dimer D (X ± s) (Me± RI)		0.13±0.60 0±0		0.23± 1.04 0± 0		0.18± 0.86 0± 0		0.21**
PCR (X ± s) (Me± RI)		67.32±94.59 28.5±94.43		84.93± 100.17 47.40± 132.19		76.71± 97.98 40.20± 114.90		0.00**

Notes: CoRad: Pulmonary involvement by tomography *Chi-square was used, **Mann Whitney U was used.

Table 5 Multivariate Analysis of Factors Associated with COVID 19 Mortality in Hospitalized Patients in La Libertad - Peru

Factors	B	Standard Error	Wald	gl	Sig.	*OR	95% C.I. for OR	
							Inferior	Superior
Age	0.034	0.005	53.937	1	0.000	1.035	1.025	1.044
Fever	−0.485	0.199	5.971	1	0.015	0.616	0.417	0.908
Productive cough	−0.410	0.180	5.161	1	0.023	0.664	0.466	0.945
Sore throat	0.274	0.125	4.782	1	0.029	1.316	1.029	1.682
Fatigue	−0.696	0.166	17.580	1	0.000	0.499	0.360	0.690
Shortness of breath	−1.079	0.119	82.534	1	0.000	0.340	0.269	0.429
Unilateral consolidation by tomography	1.370	0.542	6.386	1	0.012	3.936	1.360	11.390
Hemoglobin	−0.100	0.031	10.054	1	0.002	0.905	0.851	0.963
Leukocytes	0.000	0.000	11.557	1	0.001	1.000	1.000	1.000
Abastates	0.150	0.068	4.915	1	0.027	1.162	1.018	1.327
Lymphocytes	−0.184	0.061	9.109	1	0.003	0.832	0.738	0.937
Neutrophils	0.000	0.000	4.915	1	0.027	1.000	1.000	1.000
Platelets	−0.001	0.000	6.534	1	0.011	0.999	0.998	1.000
Urea	0.009	0.002	21.392	1	0.000	1.009	1.005	1.013
Ferritin	0.000	0.000	13.497	1	0.000	1.000	1.000	1.000

Notes: *OR: odds ratio. Model summary: Overall percentage predicted: 76%, Hosmer and Lemeshow test: Chi-Square: 0.33 (p>0.05), Cox and Snell R-square: 0.33, Nagerkerke R-square: 0.44. Area under the curve: 0.84 CI: 0.82–086 (p<0.0 5), sensitivity:75.64, specificity:77.02.

According to this model, the increase in the variables age, sore throat, unilateral consolidation tomography, leukocytes, abastonates, neutrophils, urea and ferritin constitute risk factors for mortality due to COVID-19, while fever, productive cough, fatigue, difficulty breathing, hemoglobin, lymphocytes and platelets act as protective factors.

The Hosmer and Lemeshow test indicate that the model fits the data adequately. The Cox, Snel and Nagelkerke R2 values indicate that the variables included in the model explain 32% to 43% of the mortality due to COVID-19. The prognostic percentage is 76%, which exceeds 50%, and can be considered an acceptable model. Likewise, the area under the ROC curve indicates that there is an 84% probability that the model correctly classifies COVID-19 mortality, and has an area under the curve of 0.84, CI: 0.82–086($p<0.0$ 5). In conclusion, the model has very good discriminatory capacity, 75.64% of those who died were correctly identified by the model, 77.02% of those who survived were correctly identified as such. This indicates that the model balances both important aspects for clinical prediction well.

The model has been established as follows:

Where Y: Mortality by Covid 19; X1: Age, X2: Fever, X3: Productive cough, X4: Sore throat, X5: Fatigue, X6: Shortness of breath, X7: Unilateral consolidation tomography, X8: Hemoglobin, X9: Leukocytes, X10: Abastonates, X11: Lymphocytes, X12: Neutrophils, X13: Platelets, X14: Urea, X15: Ferritine,

Discussion

An analysis of the biological factors influencing COVID-19 mortality in La Libertad Region found that most of deceased patients were male and had blood type O RH positive. However, bivariate analysis showed no significant association between sex and blood type with COVID-19 mortality. This contrasts with other findings[10,40–42] where male sex was identified as a risk factor for COVID-19 mortality. Regarding age, the average age of deceased individuals was 65.39 ±13.01 years. These findings align with those of Amatya et al[10] and Zhou et al,[41] who found the highest hospital mortality rate occurring in patients aged 56 to 65 years. This could be attributed to immune senescence in older adults, which increases susceptibility to severe COVID-19 symptoms and decreases recovery likelihood, making hospitalization fatal in many cases. Additionally, Zang[40] and Bomfim et al,[43] suggest that male sex as a risk factor for severe disease results from a combination of health-related behaviors, immune responses influenced by sex hormones and variations in Angiotensin Converting Enzyme 2(ACE2) expression between sexes.

Blood group was also found to have no significant association with mortality ($p>0.05$). However, other studies have reported that patients with blood type A face a higher risk of severe COVID-19 infection and mortality, while those with blood type O exhibit a lower risk.[44] Limachi-Choque,[19] similarly identified blood type A as a factor associated with increased mortality, independent of age, sex and comorbidities. Furthermore, individuals with blood type A, B or AB have been found to have a higher propensity for blood clot formation.[44] This, is attributed to elevated levels of von Willebrand factor and factor VIII, increasing the risk of myocardial infarction, peripheral vascular disease and venous thromboembolism.[45] Consequently, blood type may play a role in the severity of the disease and patient mortality rates.[46,47]

The relationship between comorbidities and COVID-19 mortality has also been explored in various studies. For instance, Kim et al[48] identified type 2 diabetes mellitus, hypertension, chronic kidney disease and cancer as significant factors associated with COVID-19 mortality, while no correlation was found with asthma or chronic obstructive pulmonary disease. In the case of chronic kidney disease, this study specifically determined that the association with COVID-19 mortality is present in patients at stages 4 and 5. Regarding cancer, non-alcoholic cirrhosis emerged as the condition most closely linked to COVID-19 mortality in this study.

Leulseged et al[49] found that type 2 diabetes mellitus was the most strongly associated comorbidity with COVID-19 mortality. However, in the present study no statistically significant relationship was observed ($p=0.07$). This may be due to variations in the chronicity of the disease, the degree of metabolic alterations induced by diabetes, the pharmacological treatment of diabetes, adherence to treatment and patient control measures. Likewise, non-diabetics suffering from COVID-19 were probably administered corticosteroids, which are the most commonly used drugs in the treatment of the disease during the pandemic. These drugs have the side effect of leading to a hyperglycaemic state, which is a confounding factor that could not be included in the statistical analysis because this information was unavailable, as were details of when they were administered during the infection phase and whether patients were self-medicating. These limitations add to those already mentioned above. Another group of drugs are antivirals, such as remdesivir, which is widely used in initial treatment regimens for patients with moderate and severe forms of the disease, and which also have a hyperglycaemic effect. Additionally, individuals without type 2 diabetes mellitus may have other underlying conditions, such as hypertension, chronic kidney disease or cirrhosis, which contribute to the severity of a SARS-CoV-2 infection

and mortality. Hyperglycemia, whether in patients with chronic diabetes or those experiencing the proinflammatory phase of COVID-19, has shown a strong correlation with mortality. This parameter should be considered not only in COVID-19 but also in other respiratory illnesses caused by viral infections. The excessive cytokine production during COVID-19 including IL-6 and TNF-alpha, may exacerbate insulin resistance and contribute to hyperglycemia onset.[50] Fasting hyperglycemia has been identified as an independent predictor for COVID-19 mortality, as demonstrated in multivariate analysis studies adjusting for confounding variables in Peru[51] and other countries, including patients without a prior diabetes.[52–54]

The predominant symptoms among patients who succumbed to COVID-19 varied based on individual health status and risk factors such as age, hypertension, obesity and immunosuppression primarily related to pulmonary, cardiovascular conditions, or cancer.[55,56] Table 3 highlights the signs and symptoms significantly associated with COVID-19 mortality, including fever, malaise, dry and productive cough, pleuritic pain, hemoptysis, sore throat, dyspnea, anosmia, fatigue, shortness of breath and diarrhea. These symptoms commonly align with Known COVID-19risk factors. According to WHO,[57] the most frequently reported COVID-19 symptoms were fever, chills and sore throat, while less common symptoms included persistent cough, abdominal pain, diarrhea, anosmia, fatigue and respiratory distress. Cheng et al[58] found that fever, cough, dyspnea, and chest tightness were prevalent among patients who died early in their illness, whereas diarrhea was not a distinguishing feature. Perez et al[59] reported that individuals in critical condition often presented with severe pneumonia, characterized by productive cough, fever and pleuritic pain. Similarly, Hernández R.[60] concluded that COVID-19 has contributed to high global mortality rates and is characterized by respiratory, systemic and gastrointestinal symptoms consistent with those observed in this study.

Diagnostic imagining reveals that the majority of deceased patients exhibited ground glass opacities in both lungs. These findings align with observations from a hospital in Valencia, where ground glass opacity on chest radiography was identified as a significant risk factor for hospital mortality, heart failure, respiratory failure, acute kidney injury and ICU admission.[61]

Bomfim et al[43] identified a significant correlation between mortality and pulmonary involvement, particularly ground-glass opacities, and mosaic attenuation observed in chest on CT scan. Their findings indicate that patients who succumbed to the disease were 7, 6 times more likely to exhibit lung involvement on CT than survivors ($p = 0.020$), 7.9 times more likely to present ground-glass opacities ($p = 0.017$) and 6.2 times more likely to show mosaic attenuation ($p < 0.001$).

It has been reported that lung parenchymal consolidation and ground glass opacities, two of the most commonly observed imaging features vary depending on individual patients, SARS-Cov-2 variants[62] and disease progression stages.[43] These manifestations typically emerge in the later phase of the illness (10 to 12 days) but can also occur in the early severe pneumonia cases.[63] Additionally, research suggests that older individuals experience a higher prevalence of lung lesions and ground glass opacities compared to younger adults, in whom lung parenchyma consolidation tends to be more frequent. Ground glass opacities are widely regarded as a hallmark of viral pneumonia, particularly in SARS-CoV-2 infections, whereas consolidation signals intense inflammation with the progression of CoVID-19.[62]

In terms of imagining, bilateral consolidation and CoRad 5 classification have been linked to increased mortality risk ($p<0.001$). The CoRad system, established by the Dutch Association of Radiology, categorizes pulmonary involvement based on chest CT findings, assessing severity in suspected COVID-19 cases. Prior studies indicate that higher CoRads stages correspond to increased mortality rates and greater need of ICU admission. Specifically, patients classified under CoRad 4 exhibited a threefold increased mortality risk and a twofold higher likelihood of ICU admission compared to those in CoRads1-2. Meanwhile, in CoRad 5, the odds ratios for mortality and ICU admission were 1.4 and 1.2, respectively, relative to patients in CoRad 1–2. Notably, CoRad 5 reflects greater disease severity and denotes typical COVID-19 related lung involvement.[64]

Laboratory analysis have further demonstrated that decreased hematocrit, hemoglobin, lymphocyte, and platelet levels were associated with mortality in COVID-19 patients ($p<0.001$). This aligns with findings from previous studies, which indicated that older age, elevated neutrophil-to-lymphocyte ratios and increased white blood cell counts were linked to heightened mortality risk.[65] Additionally, research has shown that critically ill patients exhibit significantly reduced lymphocyte counts, suggesting substantial immune cell consumption, thereby compromising immune function.[66] Lymphocyte depletion may stem from factors such as bone marrow suppression, cytokine storm induced apoptosis, increased lymphocyte destruction, sequestration in lung tissue, and severe acidosis associated with COVID-19.[66,67]

Given their critical role in both cellular and humoral immunity, lymphocytes tend to decline in prolonged inflammatory states. In addition, lymphocytes are responsible for destroying virus-infected cells.[66] Consequently, lymphocyte depletion could serve as a key indicator in assessing disease severity.[68]

The literature indicates that decreased platelet levels during disease progression may serve as a predictor of severe cases and poor outcomes.[43] However, platelet levels can also rise during an intense cytokine storm, leading to a relative excess that elevates platelet-to-lymphocyte ratio an independent marker of prolonged hospitalization and adverse clinical outcomes in COVID-19. These platelet irregularities may contribute to coagulation disorder, which can manifest as thrombotic events in multiple vascular beds and are often accompanied by high D-dimer values.[67] In patients with severe COVID-19 pneumonia D-dimer values trend to increase significantly and are consider predictive markers of both clinical severity and mortality.[69] However, in this study, D-dimer levels were not found to be significantly associated with mortality ($p>0.005$), likely due to the implementation of therapeutic anticoagulation as a standard component of COVID_19 management.[70]

This investigation also identified higher mean values of leukocyte counts, abastonates, neutrophils, creatinine, urea, ferritin and C-reactive protein (CRP) in deceased patients compared to survivors, all of which were linked to COVID_19 related mortality.[71] Additionally, mortality was associated with elevated levels of CRP, interleukin-6, lymphocytes, neutrophil-to-lymphocyte ratio, platelets, hemoglobin, iron, total iron binding capacity, ferritin, D-dimer ($p < 0.005$). This contrasts with findings by Yildirim et al,[64] who reported no significant association between fibrinogen, ferritin, lymphocyte and mortality. However, prior studies have suggested that increased neutrophil counts, CRP, and procalcitonin in patients with severe or critical COVID-19 may be indicative of a cytokine storm triggered by viral invasion or concurrent infections.[68]

A pronounced elevation in neutrophils has been linked to cytokine storm and tissue damage, contributing to severe pneumonia and mortality, as observed in SARS and MERS cases. Neutrophilia may partially correlate with disease progression, ICU admission, higher mechanical ventilation requirements, and increased mortality risk in COVID-19 patients with elevated white blood cell counts.[70]

Furthermore, in line with findings Guimaraes by et al,[72] this study also observed increased abastonate counts in deceased patients. Elevated levels of immature leukocytes may contribute to a dysfunctional innate immune response, exacerbating lung damage and worsening patient outcomes.

Ferritin, a biomarker of iron metabolism and inflammation, plays a crucial role in immune modulation and influences the susceptibility to viral infections. It serves as an indicator of myeloid cell activation in both blood and inflamed tissue and is released from activated macrophages and hepatocytes to protect cells from oxidative damage while sequestering iron from pathogens. Once released, ferritin can further stimulate macrophages promoting the production of cytokines such as IL-6 and IL-1β, thereby sustaining a positive feedback loop of proinflammatory responses. Elevated IL-6 and ferritin levels have been linked to increased disease severity, and may serve as predictors of mortality.[71]

C-reactive protein (CRP) plays a significant role in predicting the worsening of COVID-19 symptoms. As an essential marker of inflammation, CRP contributes to the body's defense against infectious agents and may serve as an indicator of pulmonary disease exacerbation. In patients with SARS-CoV-2 infection, elevated CRP levels have been linked to a higher incidence of lung lesions and weight loss.[73]

Furthermore, deceased patients exhibited increased average levels of urea and creatinine. In a study by Mirmohammadi et al,[74] assesments of renal function in COVID-19 patients, focused primarily on proteinuria, urea and creatinine levels. The findings revealed an incidence of acute kidney injury ranging from 3% to 9% among individuals infected with SARS-CoV-2. Another study reported that among 710 hospitalized COVID-19 patients, 44% had proteinuria, while 15.5% and 14.1% exhibited elevated serum creatinine and blood urea nitrogen, respectively.[75] These renal complications are largely attributed to virus's ability to find ACE2 receptors expressed in renal tissue.[42]

De La Torre et al[76] further observed that elevated creatinine and urea levels were associated with cardiac arrhythmia and acute inflammatory state COVID-19 in patients. Notably, renal impairment is common among individuals with COVID-19, particularly in elderly patients undergoing dialysis, which predisposes them to increased urea, creatinine levels and hypercatabolism.[73]

Multivariate analysis using a logistic regression model identified older age as a significant risk factor for COVID-19 mortality, aligning with findings from a study conducted in Spain, where deceased patients were notably older (mean age of 77 years) compared to survivors.[77]

Additionally, a study in Peru identified age, sex, cough, respiratory difficulty and diabetes as mortality risk factors.[78] However, in this study, productive cough was not included in the model as a risk factor. In COVID-19 patients, this symptom often persists as a residual effect following infection. Fever and dyspnea were also observed to decrease the risk of mortality when treated promptly.[79]

Several studies have reported that unilateral consolidation as evidenced by computed tomography signifies severe pulmonary involvement and increased risk of death in COVID-19 patients.[64,65] Leukocytosis, including increased abastonates and neutrophils, is commonly observed in systemic infection, making these factors potential predictors of mortality.[69,70]

Elevated blood urea levels may indicate various medical conditions. Typically, urea is excreted as part of protein metabolism; however, COVID-19 related renal impairment can lead to urea retention in the bloodstream, thereby increasing mortality risk.[75] Additionally, excessive ferritin levels, indicative of iron overload, have been identified as risk factors for COVID-19 mortality.[71]

Conversely, hemoglobin, lymphocytes and platelets were found to act as protective factors. This may be explained by the association between normal hemoglobin levels in both men and women and a reduced risk of mortality. Lymphocytes play a crucial role in immune defense against viral infections, while platelets are affected by the hypercoagulability. Consequently, anticoagulant therapies have been implemented to mitigate the risk of mortality due to thrombosis.[67]

One limitation of this study was the possibility of data entry errors by the on-call healthcare personnel. However, a rigorous quality control process was implemented to ensure data integrity. Another limitation is the lack of knowledge about the types of virus variants that infected the patients, as treatment, symptoms, and biochemical and clinical parameter values vary according to the infectiousness of the variant, whose influence on mortality could be significant.

Furthermore, because this was a retrospective study, non-biological factors such as socioeconomic status, health literacy, availability of hospital services, and other social determinants were not considered. However, we recognize their potential influence and emphasize the need for future research to systematically address them. The model showed good internal fit and acceptable explanatory capacity; however, its performance was not evaluated in an independent cohort, so its applicability in other contexts or populations cannot be guaranteed. Future studies could conduct external validation in cohorts from other regions of the country or in later periods of the pandemic, which would confirm the robustness and generalizability of the model. This validation is essential for its potential implementation as a tool to support clinical decision-making.

The strength of this study is that it provides a significant contribution by comprehensively analyzing a wide range of biological, clinical, laboratory, and imaging factors associated with COVID-19 mortality in the La Libertad region, an area with unique sociodemographic and health characteristics within the Peruvian context. The findings are consistent with the international literature on the main risk factors, such as advanced age, the presence of comorbidities, and certain inflammatory and hematological markers. We recognize that the evolution of clinical protocols and the impact of vaccination have modified mortality factors in later phases. However, the data analyzed provide an important basis for understanding the initial behavior of the virus and associated factors in that context, providing valuable information for historical epidemiology and for planning for future health emergencies.

Conclusion

The results indicate that the model is effective in identifying risk factors for COVID-19 mortality, with the most significant predictors being advanced age, sore throat, unilateral consolidation observed in tomography, leukocytes, abastonates, and neutrophils counts, urea and ferritin levels. The Cox and Snell R-squared coefficients of determination demonstrate an acceptable level of explanatory power, reflecting a substantial percentage of variance explained. The model accurately classifies 76% of cases.

Data Sharing Statement

Research data are available upon request.

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Author Contributions

All authors made a significant contribution to the reported work, either in the conception, design, execution, data acquisition, analysis, and interpretation, or in all of these areas; participated in the writing, revision, or critical review of the article; gave final approval of the version to be published; agreed on the journal to which the article was submitted; and agree to be responsible for all aspects of the work.

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Disclosure

The authors declare no conflicts of interest in this work.

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