

## Original Research

# RISK FACTORS FOR MORTALITY IN ADULT PATIENTS WITH COVID-19 IN NORTHEAST MEXICO

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**Abstract: Introduction.** The pandemic, in terms of incidence, mortality, speed of expansion, the clinical presentation of a disease, and severity, is heterogeneous between regions of the same country. For this reason, the research aims to establish the risk factors associated with mortality in adult patients with COVID-19 in northeast Mexico.

**Material and methods.** The retrospective cohort study included hospitalized patients older than 18 years diagnosed with COVID-19 through RT-PCR test. Data were collected from the electronic medical records and analyzed to detect differences between survivors and non-survivors, using Student's t-test and Chi-square or Fisher's exact test. The relative risk was calculated with a 95% confidence interval (with statistical significance  $p < 0.05$ ).

**Results.** Two hundred forty-seven patients were studied with a mortality of 50.2%. Arterial hypertension was the most frequent comorbidity. The oxygen supply with an invasive device was associated with a high risk of death. Tracheostomy is a high-risk factor ( $p < 0.001$ ) of mortality prediction. The patients who required only a mask and the nasal cannula showed a better survival ( $p < 0.05$ ). The most frequent symptoms were dyspnea, fever, and cough without statistical difference among the study groups (patients who were discharged alive from the hospital and those deceased). Sat O<sub>2</sub> at admission showed a significant difference between both groups.

**Conclusion.** Risk factors could predict mortality in patients with COVID-19. A peripheral SatO<sub>2</sub> of  $< 90\%$  at admission and the determination of brain natriuretic peptide and D-dimer warrant close monitoring to avoid severe complications.

**Main messages** The study shows the clinical and laboratory risk factors, which predict disease outcomes of patients diagnosed with COVID-19 in a tertiary hospital in northeastern Mexico. The results allowed precision in early detection and decision-making in patients with SARS-CoV-2. The limitations of this study are the size of the population.

## INTRODUCTION

The COVID-19 disease (coronavirus disease 2019) caused by the coronavirus SARS-CoV 2 (Severe Acute Respiratory Syndrome) was first reported in China in December 2019 and 11 months later has been extended worldwide with

61, 869,330 confirmed cases [1]. Currently, some regions in the world are showing a downward trend in new cases; however, Europe is the largest contributor of deaths in recent weeks, and the Americas reported an increase in new cases of deaths, which is why this disease is currently considered to have the highest proportion of accumulated cases and deaths [2].

Control measures have been established since the COVID-19 outbreak became known in Mexico. By January 9, 2020, the General Directorate of Epidemiology issued a

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preventive travel notice to China. Shortly after, the standardized guideline was published for epidemiological and laboratory surveillance by nCov-2019, in which operational definitions were established and still subject to change. And for February 28 of the same year, the INDRE (Institute of Epidemiological Diagnosis and Reference) confirmed the first case of COVID-19 in Mexico. By November 22, 2020, 28,576 new cases were reported in the country, 1,025,969 confirmed with 782 deaths per million people. In the Americas region, it ranks third in the number of deaths only after the United States and Brazil. Its epidemic behavior worries nationally and internationally, an important advance has been generated in scientific evidence, but there are still many questions to be answered. Since there is currently no specific treatment, the prevention and control measures recommended by the World Health Organization (WHO) should be continued [3].

Currently, in light of the scientific knowledge of COVID-19, by SARS CoV2, some researchers have found differences in its clinical presentation, the severity of the disease and mortality; age and present comorbidities play a very important role in this last data [4], without forgetting that affected patients require health care and hospitalization so that the technological and scientific infrastructure and the capacity of the health system in each country are of great importance in the impact of the pandemic [5]. In Mexico, epidemiological studies of COVID-19 have been implemented, but there are no reports on this issue in our region. The population has demographic and ethnic differences with respect to central and southern Mexico. The hospital infrastructure and human resources are limited compared to other regions in the northern part of the country [6].

Risk factors that are related to the morbidity and mortality of COVID-19, especially age, sex, and comorbidities, have been described in the literature [7]. Therefore, the objective is to know the risk factors associated with mortality in adult patients with COVID-19 in northeast Mexico.

#### **METHODOLOGY**

The retrospective cohort study included patients older than 18 years of age at the Hospital Regional de Alta Especialidad "BICENTENARIO 2010" in Victoria Tamaulipas, Mexico, from April 1 to November 30, 2020.

The patients were diagnosed with COVID-19 according to the positive results of the RT-PCR (Reverse transcription-polymerase chain reaction) test. This study was accepted

by the Ethics and Research Committee of our Hospital with the number: HRAEV-IC-002-21.

The epidemiological, demographic, clinical, laboratory, management, and treatment information were obtained from the electronic medical records according to the official Mexican standard of each patient's clinical record NOM-004-SSA3-2012 [8]. All the results of the confirmatory tests for SARS-CoV-2 were obtained from throat and nasopharynx swabs by the epidemiology service of a referral hospital and confirmed by our hospital.

The hospital discharge criteria were the absence of fever for 72 hours, Computed Axial Tomography (CT) of the chest with improvement in both lungs, clinical improvement in respiratory symptoms, and two negative throat and nasopharynx swabs for SARS-CoV-2 obtained at least 24 hours apart. Routine blood tests were: complete blood count, coagulation tests, serum biochemistry [kidney and liver function, creatine phosphokinase (CPK), lactic dehydrogenase, complete electrolytes], myocardial enzymes, interleukin-6 (IL-6), serum ferritin, brain natriuretic peptide (BNP), and procalcitonin. Images study included: chest X-rays, Computed Axial Tomography, or Nuclear Magnetic Resonance for all patients in the study.

Fever was considered when an axillary temperature was greater than 38° C. Sepsis and septic shock were confirmed and defined according to Clinical Practice Guidelines [9]. Secondary infection was identified when patients had clinical symptoms of pneumonia or bacteremia and a lower respiratory tract culture, endotracheal aspirate, or bronchoalveolar lavage. Ventilator-associated pneumonia refers to the fact that it is acquired after 72 hours of endotracheal intubation in a patient undergoing mechanical ventilation; it must include: new or progressive infiltrates, consolidation, cavitation or pleural effusion in the chest radiograph, and at least one of the following: purulent sputum or changes in the characteristics of sputum, fever, increase or decrease in the white blood cell count, microorganisms cultured in blood, or identification of a microorganism in bronchoalveolar lavage or biopsy [10, 11]. Acute kidney injury was defined according to the KDIGO [12] clinical practice guidelines, and acute respiratory distress syndrome (ARDS) was diagnosed according to the Berlin definition [13]. The acute cardiac injury was considered if the serum levels of cardiac biomarkers (including troponin) were above the upper limit 99th percentile or if abnormalities were seen in the electrocardiogram, clinical data, and echocardiogram. The severity of the COVID-19 disease was defined according to the management guidelines for COVID-19 [14].

Coagulopathy was defined as a lengthening of more than 3 seconds of the prothrombin time or more than 5 seconds of the activated partial prothrombin time. Hypoproteinemia was defined as a serum level of albumin below 25 gr/L.

#### Data Collection and Statistical Analysis:

The information was collected through a specific data card for the project. A data capture document was anonymous with a unique encoding. Once all the data were collected from the Electronic Medical Record, the data collection sheets were compared with the database using the SPSS version 25 statistical program.

Socio-demographic groups, incidence, and mortality rates were calculated from the number of confirmed cases and deaths (non-survivors) from COVID-19 using the state and/or national populations for the denominators. The fatality ratio was calculated as the proportion of people who died from the disease to the total number of people diagnosed with it. The measurement was used to assess both the mortality of an outbreak and the public health situation in a specific area [15].

A bivariate analysis was performed to detect differences between survivors and non-survivors (deceased). The Student's t-test was used for continuous variables and Chi-square or Fisher's exact test for categorical variables. Descriptive statistics techniques, means, percentages, and standard deviation were applied. The relative risk was calculated with a 95% Confidence Interval (95% CI), and statistical significance was considered with a value of  $p < 0.05$ .

We used the difference of means for two independent groups, Levene's test for the difference in variance and Student's test if the variance was homogeneous with homoscedasticity, and Welch's test for heterogeneous or heteroskedastic variances. Data analysis was performed using the SPSS version 25 statistical program.

#### RESULTS

Two hundred forty-seven patients diagnosed with COVID-19, confirmed by the nasal and retropharyngeal swab RT-PCR test, were studied. Among them, 123 (49.79%) survived, and 124 (50.2%) did not survive; of the patients who survived, 50 (40.7%) were females and 73 (59.3%) males. Of the 124 that did not survive, 40 (32.3%) were females, 84 (67.7%) males, the fatality ratio was 50.2%.

According to a referral place ( $n = 247$ ): 29.55% ( $n = 73$ ) came from home, 70.45% ( $n = 174$ ) came from a medical

institution. According to the hospital admission service: 64% ( $n = 157$ ) were admitted to the COVID dedicated hospital floor; among those patients 50% ( $n = 62$ ) did not survive, presenting a mortality rate of 39.24%. Thirty three percent ( $n = 81$ ) were admitted to the adult intensive care unit (ICU), 45% did not survive ( $n = 56$ ) and had a fatality of 65.88%; 4% ( $n = 9$ ) were admitted to the emergency room, 5% ( $n = 6$ ) did not survive with a fatality of 75%.

When divided according to age, of all admitted with COVID-19 patients, the group of 18 to 59 years of age ( $n = 126$ , 51.01%) was numerically identical to the group of patients 60 years and over ( $n = 121$ , 48.99%).

Table 1 presents the relative risk (RR) with the respective 95% confidence intervals (95% CI) for sex and age in years. With respect to sex, there was no statistical difference in the p-value or the RR, but there was an increase in the RR of not surviving as age increased. Table 1 also presents the most frequent comorbidities detected in patients with COVID-19. We observed that the most frequent comorbidity was arterial hypertension, with a statistical difference by the p-value and a higher RR for non-survivors. When considering the number of comorbidities, it was striking that having two or more substantially increased the risk of dying.

Such symptoms as dyspnea, fever, and cough were presented with the same frequency in survived and deceased patients (Table 2).

Table 3 shows the oxygen supply with its different devices, surgical techniques such as tracheostomy, hospitalization area, and the number of days staying in the hospital. The relative risk of not surviving patients increases when an invasive device and surgical procedure (tracheostomy) is used. With a very significant increase in the relative risk when this procedure is performed late. According to the hospitalization area, the relative risk for not surviving increases in the intensive care unit, which is expected by the severity of the patients.

In Table 4, we present the difference in means for two groups with respect to the inflammatory markers. However, there were no statistical differences for ferritin in the three markers we studied. Still, nevertheless, for the D-dimer and the marker Pro brain Natriuretic peptide (Pro-BNP), we found statistical differences, so they can be considered excellent markers of severity.

We did not find a statistical difference or increase in relative risk regarding referral place. According to the

length of hospitalization, we detected that the risk of not surviving from the group of 4 to 7 days increased. It is striking that the risk of not surviving significantly

decreased in the group of 1 to 3 days. When comparing the means of the arterial oxygen saturation values at admission, statistical significance was detected (Table 5).

Variables	Survived n=123		Deceased n=124		Relative Risk (RR)	Confidence Interval CI (95%)	P value
	n	%	n	%			
<b>Sex</b>					<b>0.83</b>	<b>(0.63 to 1.09)</b>	<b>0.17</b>
Male	73	59.34	84	67.74	1.20	(0.92 to 1.58)	0.17
Female	50	40.65	40	32.25	0.83	(0.63 to 1.09)	0.17
<b>Age</b>							
18-21	6	4.88	0	0.00	0.11	(0.00 to 53.98)	0.34
22-44	43	34.95	8	6.45	0.29	(0.15 to 0.59)	0.00
45-49	17	13.82	7	5.64	1.86	(0.76 to 4.53)	0.17
50-59	21	17.07	24	19.35	3.40	(1.70 to 6.79)	0.00
60-64	18	14.63	19	15.32	3.27	(1.61 to 6.65)	0.00
65-70	9	7.31	24	19.35	4.64	(2.37 to 9.06)	0.00
71-80	4	3.25	26	20.96	5.53	(2.88 to 10.60)	0.00
81-90	5	4.00	15	12.09	4.78	(2.41 to 9.48)	0.00
91-100	0	0.00	1	0.80	6.38	(3.37 to 12.05)	0.50
<b>COMORBIDITY</b>							
*AH	43	34.95	66	53.22	1.44	(1.12 to 1.85)	0.004
**MD	40	32.52	65	52.41	1.49	(1.16 to 1.91)	0.002
Obesity	19	15.44	33	26.61	1.36	(0.05 to 0.75)	0.03
***CKD	4	3.25	14	11.29	1.62	(0.22 to 2.15)	0.01
Dyslipidemias	3	2.43	6	4.83	1.34	(0.83 to 2.17)	0.31
Asthma	2	1.62	1	0.80	0.66	(0.13 to 3.29)	0.55
Cancer	1	0.81	1	0.80	0.99	(0.24 to 4.00)	0.99
Heart disease	1	0.81	1	0.80	1.01	(0.24 to 4.00)	0.99
****COPD	1	0.81	2	1.61	1.33	(0.59 to 2.99)	0.56
Steatosis	1	0.81	1	0.80	1.00	(0.24 to 4.00)	0.99
<b>Number of Comorbidities</b>							
1 comorbidity	32	26.00	39	31.50	2.04	(1.34 to 3.11)	0.00
2 comorbidities	18	14.60	39	31.50	2.54	(1.69 to 3.81)	0.00
3 or more comorbidities	16	13.00	25	20.20	2.26	(0.45 to 3.51)	0.00
Without comorbiditis	57	46.30	21	16.90	0.44	(0.30 to 0.65)	0.00

\*AH: Arterial hypertension

\*\*MD: Mellitus diabetes

\*\*\*CRI: Chronic kidney disease

\*\*\*\*COPD: Chronic obstructive pulmonary disease

Source: Epidemiology, Regional Hospital of High Specialty "Bicentenario 2010", Pediatrics Division, Ciudad Victoria, Tamaulipas, Mexico

**Table 1. Distribution by sex, age, and comorbidity of all patients (survived and deceased) with their respective relative risks, 95% confidence intervals, and p <0.05.**

Symptoms	Survived n=123		Deceased n=124		Relative Risk (RR)	Confidence Interval CI (95%)	P value
	n	%	n	%			
Dyspnoea	93	75.5	104	83.87	1.32	(0.91 to 1.90)	0.10
Fever	68	55.28	57	45.96	0.83	(0.65 to 1.06)	0.14
Cough	42	34.14	48	38.70	1.10	(0.86 to 1.42)	0.45
General discomfort	29	23.57	26	20.96	0.92	(0.67 to 1.26)	0.62
Myalgia	25	20.32	33	26.61	1.18	(0.90 to 1.54)	0.24
Arthralgias	22	17.88	26	20.96	1.10	(0.81 to 1.47)	0.54
Asthenia	22	17.88	17	13.70	0.84	(0.57 to 1.24)	0.36
Odynophagia	18	14.63	17	13.70	0.96	(0.66 to 1.38)	0.83
Adinamia	24	19.51	20	16.12	0.88	(0.62 to 1.26)	0.48
Headache	21	17.07	17	13.71	0.87	(0.59 to 1.27)	0.46
Diarrhea	12	9.76	10	8.06	0.89	(0.55 to 1.44)	0.64
Fatigue	7	5.69	8	6.45	1.06	(0.65 to 1.74)	0.80
Chest pain	5	4.06	6	4.83	0.09	(0.62 to 1.89)	0.76
Rhinorrhea	4	3.25	3	2.41	0.85	(0.35 to 2.01)	0.69
Anosmia	3	2.43	4	3.22	1.14	(0.59 to 2.19)	0.70
Abdominal pain	3	2.43	2	1.61	0.79	(0.26 to 2.33)	0.64
Eye pain	2	1.62	1	0.8	1.66	(0.13 to 3.29)	0.55
Ageusia	0	0.00	3	2.42	2.01	(1.77 to 2.28)	0.08

n: number of patients

#: percentages

Source: Epidemiology, Regional Hospital of High Specialty "Bicentenario 2010", Pediatrics Division, Ciudad Victoria, Tamaulipas, Mexico.

**Table 2. Most frequent symptoms in patients with COVID-19.**

## DISCUSSION

In this COVID-19 study, the behavior of the SARS-CoV-2 coronavirus infection was compared in patients who did not survive against survivors. When studying sex differences, greater mortality was observed in the male population (67.74%). Other researchers have reported a greater affectation for the male sex; however, they have not found a statistically significant association may be due to the fact that men have a greater genetic predisposition to contract diseases and are biologically different from women, therefore the immune response is different [16-19].

With respect to age, the risk of dying from COVID-19 increases with aging; previously, it has been reported that old age is an important independent predictor of mortality in severe acute respiratory syndrome (SARS) and

syndrome of Middle East Respiratory Disease (MERS); in the present study, it was found that after 50 years of age the risk of not surviving increases with statistical significance [20]; a younger age is a protective factor to survive since younger people have fewer comorbidities: that was confirmed by other authors [19,21].

Regarding comorbidities in both groups of survivors and non-survivors, the vast majority had between one and two comorbidities: diabetes mellitus, hypertension, and obesity. A statistically significant association between mortality and comorbidities was detected with the increased number of comorbidities, the risk of dying increases, which other researchers confirmed [16,20,21].

The level of the decline of oxygen saturation at hospital admission of all COVID-19 patients was associated with



Variables	Survived		Deceased		Relative Risk (RR)	Intervalo de Confianza IC (95%)	p valor
	n	%	n	%			
<b>Oxygen supply</b>							
Intubation	24	19.50	92	74.20	3.25	(2.37 to 4.45)	0.00
Reservoir Mask	20	16.30	6	4.80	0.43	(0.21 to 0.88)	0.00
Nasal Tips	53	43.10	5	4.00	0.14	(0.06 to 0.32)	0.00
Tracheotomy	4	3.30	21	16.90	1.81	(1.45 to 2.26)	0.00
<b>Tracheotomy</b>							
early <10 days	1	0.80	3	2.4	1.51	(0.84 to 2.69)	0.31
late > 10 days	3	2.40	18	14.5	1.83	(1.46 to 2.28)	0.00
<b>Hospitalization area</b>							
Admission	3	2.40	6	4.80	1.34	(0.83 to 2.17)	0.31
Intensive care unit	25	20.30	56	45.20	1.69	(1.34 to 2.13)	0.00
COVID-19 hospitalization	95	77.20	62	50.00	0.57	(0.45 to 0.73)	0.00
<b>Days Stay</b>							
1-3	47	38.21	12	9.67	0.45	(0.25 to 0.81)	0.00
4-7	29	23.57	24	19.35	2.22	(1.24 to 3.99)	0.00
8-15	31	25.20	47	37.90	2.96	(1.73 to 5.06)	0.00
16-30	13	10.56	35	28.22	3.58	(2.10 to 6.11)	0.00
31-41	2	1.62	3	2.41	2.95	(1.22 to 7.08)	0.04
42-52	1	0.81	2	1.61	3.27	(1.27 to 8.44)	0.06
53-63	0	0.00	1	0.80	4.91	(2.96 to 8.35)	0.55

n: number of patients

%: Percentage

ISSSTE: Institute of Social Security and Services for State Workers

Source: Epidemiology, Regional Hospital of High Specialty "Bicentenario 2010", Pediatrics Division, Ciudad Victoria, Tamaulipas, Mexico.

**Table 3. Oxygen delivery techniques, tracheostomy, hospitalization area and hospital stay days.**

mortality: a statistically significant association of oxygen saturation and mortality was found [21,22]. The arterial oxygen pressure decreased when the pathology was identified; the oxygen saturation measured peripherally was used to continuously analyze the oxygenation in blood to approximate the arterial partial pressure of oxygen. Most patients admitted to the hospital did not have a blood gas record. Therefore, peripheral oxygen saturation at admission was used as a variable in the study; low oxygen saturation was statistically associated with the risk of dying [23].

The oxygen delivery devices to patients such as a nasal cannula, reservoir mask, intubation, and tracheostomy

were considered factors associated with mortality. A lower risk ratio of death was observed when a non-invasive device was used, and an increased risk with invasive procedures: intubation and tracheostomy with statistical significance. It is very important to understand the use of which oxygen device is associated increases the risk of dying [21, 23]. This finding gives the guideline to modify the respiratory management scheme and use less invasive airway devices, if possible, to improve survival [22]. When reviewing invasive procedures such as tracheostomy, both groups of survivors were compared with non-survivors; considering the time in which the procedure was performed, either early <10 days or late > 10 days, we found that the risk of dying was statistically significant when the tracheostomy was done late [22,23].

Variables	Survived (n=123)		Deceased (n=124)		Difference of means CI (95%)	P for difference of means	Contrast power %
	μ	DE	μ	DE			
<b>D-dimer (0-400ng/ml)</b>							
Admission	1112.79	1819.93	2298.27	2456.48	1186 (638.89 to 1732.11)	0.0000	100
Hospital stay	791.51	1788.05	1534.90	2010.12	743.39 (263.82 to 1222.96)	0.0025	99
Discharge	266.13	647.81	1243.24	1897.34	977.11 (617.26 to 1336.96)	0.0000	100
<b>Ferritin (17.9-464 ng/ml)</b>							
Admission	596.33	1185.59	871.80	1191.69	275.47 (-25.57 to 576.51)	0.07	71.9
Hospital stay	205.72	838.67	284.70	620.40	78.98 (-106.63 to 264.59)	0.40	10.4
Discharge	87.45	794.11	189.38	974.85	101.93 (-121.38 to 325.24)	0.36	32.5
<b>Pro-BNP (&lt; 100 ng/L)</b>							
Admission	285.70	590.90	1417.86	2870.08	1132.16 (600.87 to 1663.45)	0.0000	100
Hospital stay	171.30	546.16	989.56	2300.10	818.26 (388.05 to 1248.47)	0.0003	100
Discharge	101.32	409.65	907.30	1899.70	805.98 (450.87 to 1161.09)	0.0000	100

μ: half

DE: Standard deviation

\*ProBNP: brain natriuretic peptide

\*\*N: number of patients

\*\*\*%: Percentage

Source: Epidemiology, Regional Hospital of High Specialty "Bicentenario 2010", Pediatrics Division, Ciudad Victoria, Tamaulipas, Mexico.

**Table 4. Difference in D-Dimer, Ferritin, and \* NT-ProBNP between two groups (survived and deceased patients) upon admission, during hospitalization, and discharge.**

Recommendations from previous experiences in China do not establish a better approach to tracheostomy in patients with COVID-19. Some doctors recommend not doing a tracheostomy before three weeks because of the great transmission of the virus and the poor prognosis reported by the invasive procedure [24,25].

Some researchers have implemented protocols to improve survival in these patients, avoiding the risk of complications as much as possible using specific protocols and safe procedures [26,27]. We report that mortality in Covid-19 patients is very high (84%). A few risk factors are

involved: age, the severity of lung injury, comorbidities, delay inpatient admission, and protocols in tracheostomy surgical procedures [28, 29].

The association of death according to the hospitalization area: admission (emergency), hospitalization-COVID-19 to the designated floor, and adult intensive care unit (ICU) - the risk of dying increases significantly in the ICU and in the hospitalization area-Covid-19 [30]. Mortality may be related to personal, professional training, the duration of a patient hospital stays, technology, and infrastructure

Variables	Survived (n=123) %	Deceased (n=124) %	P value of difference of means	Difference of stockings CI (95%)	D by COHEN	Levene's test	Contrast power %
SatO2	90.07 (DE: 10.28)	84.04 DE:(14.73)	0.00	-7.96 (-11.17 a - 4.75)	-0.63 (-0.88 a - 0.38)	0.00	100
Days	Survived (n=123)	Deceased (n=124)	Relative Risk (RR)	Confidence interval CI (95%)		p value	
1 to 3	6	12	1.36	(0.96 to 1.94)		0.14	
4 to 7	40	39	0.98	(0.75 to 1.28)		0.85	
8 to 11	46	23	0.59	(0.41 to 0.84)		0.001	
12 to 16	22	33	1.27	(0.97 to 1.65)		0.09	
17 to 20	3	8	1.48	(1.01 to 2.17)		0.12	
21 to 26	4	5	1.11	(0.61 to 2.02)		0.74	
27 to 30	0	0	0	(0.00 to 0.00)		0	
31 to 40	1	2	1.33	(0.59 to 3.00)		0.56	
41 to 44	1	2	1.33	(0.59 to 3.00)		0.56	

DE: Standard deviation

Source: Epidemiology, Regional Hospital of High Specialty "Bicentenario 2010", Pediatrics Division, Ciudad Victoria, Tamaulipas, Mexico.

**Table 5. Difference in oxygen saturation at admission, and time from onset of symptoms to hospitalization of patients with COVID-19 between two groups (survived and deceased patients).**

that is more relevant to low-income communities [29,30,31].

Concerning symptoms, most researchers agree that the three main symptoms of COVID-19 are: fever, cough, and dyspnea. When comparing the symptoms of both groups of survivors against non-survivors, no statistically significant association with mortality was found. The latter had the purpose of knowing early some symptoms as a prognostic risk factor that allows early identification of patients with a fatal outcome. We did not find a statistical difference, possibly due to the stage at which Covid-19 was diagnosed in our patients' population [22,23]. However, dyspnea is the only symptom that significantly predicts severe disease and can discriminate between patients admitted to the ICU [32,33], although we believe that the size of the population studied affected our findings.

When reviewing a place of reference as a variable associated with severity or death, the vast majority of patients arrived from their homes. They were also patients referred from some hospital institutions in the city and different regions of the state, but there was no statistical

difference. In many parts of the world, this parameter is vital; its identification, isolation, management, and prompt admission to hospital play a crucial role in the survival of patients [22, 34]; early diagnosis, confirmation, and evaluation by a medical professional are important, transfer it to a hospital institution is very important since it can reduce mortality.

Regarding the hospital stay in both groups of survivors versus non-survivors, it was found that the risk of dying increases with the number of days of hospitalization with statistical significance, except in the group of 42 to 63 days where no statistically significant association was confirmed; the findings are very similar to what was stated by other researchers [19,35].

Predictors of a fatal outcome in COVID-19 include, among others: age, comorbidities, aggregate infections, and inflammatory indicators: D-dimer, ferritin, and brain natriuretic peptide (BNP) to alert the clinician and effectively prioritize resources and management of patients at higher risk. The same markers that identify the cytokine storm syndrome activated by the SARS-CoV-2



[36] virus was measured at admission, during hospitalization, and at discharge. The D-dimer level was statistically significantly different between survivors and deceased at admission, during hospitalization, and at discharge, so it should be considered a strong predictor of poor prognosis. No statistical significance was observed for ferritin, although its results could be altered. For the BNP, statistically significant differences could be confirmed in the three-time points values, which is why it is also a strong predictor of poor prognosis [37, 38]; the markers were significantly higher in the non-survivor groups than in the survivor groups. The findings show that ferritin could be elevated due to several factors; this marker is elevated in other pathologies: hematological malignancies, liver failure, infections, renal failure, hemoglobinopathies, chronic transfusions, and hemophagocytic histiocytosis [37,38].

We studied an association between these parameters and mortality regarding the time from onset of symptoms to admission to the hospital. We did not find a statistical difference between the two groups. Therefore, no differences were found in this indicator, and an attempt was made to stratify it into groups. If the patients arrive between the eighth and eleventh day, the possibility of survival is greater; no significant statistical difference was confirmed in other groups [19,22,39].

#### Study limitations

The size of the study population is small; in addition to being a retrospective study, it reduces the impact of the work; the laboratory markers of the study were only limited to three of them considered as the most representative since more markers could help in future research.

#### Conclusion

Risk factors of age over 60 years, more than two comorbidities, systemic arterial hypertension, peripheral oxygen saturation less than 90% upon admission, needs for invasive devices to administer oxygen, late tracheostomy are factors that merit close monitoring in patients with COVID-19.

#### Author contributions

OMBB, PRV, JAVS, AAM, HZG, SGME, VEFR and research designed by OMBB, PRV; performed the review and editing, OMBB, PRV, JAVS, AAM, SGME; VEFR, HZG provided the acquisition of funds, the administration of the project and the resources; and OMBB, PRV wrote the article.

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