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Confirmed SARS-CoV-2 infection and mortality: Associated factors in hospitalized people 75 and older

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ABSTRACT

Introduction: COVID-19 infection in the elderly posed challenges in health systems and clinical care by health personnel.

Objective: To describe the factors associated with mortality in persons aged 75 and older with COVID-19 in a high complexity hospital in Bogotá, Colombia.

Methods: Observational, analytical and retrospective study, including 509 patients aged 75 and older hospitalized with COVID-19.

Results: 40.47% died during hospital stay. It was found that a shorter time of symptom onset at admission, a respiratory rate greater than 20 breaths per minute, having thrombocytopenia, elevated lactate dehydrogenase and elevated D-dimer were associated with higher in-hospital mortality.

Conclusions: There is an association between mortality and the presence of dyspnea, fever and delirium. Paraclinical results with lactate dehydrogenase >350 (U/L), the presence of elevated D-dimer greater than 1,000 µg/L, as well as a Pa02/Fi02 ratio with a median of less than 90, were associated with higher mortality.

Keywords: Coronavirus infections, SARS-CoV-2, elderly, mortality

INTRODUCTION

In December 2019, a group of patients suffering from severe pneumonia of unknown cause was documented in the Chinese city of Wuhan, Capital of Hubei Province, alerting local health authorities. As an epidemiological link, these affected subjects worked in or had some close contact with the city's live species market [1]. The pathogen producing this infectious condition was identified as a new enveloped RNA *betacoronavirus*, which has been currently referred to as severe acute respiratory syndrome (SARS-CoV-2), similar to that caused by SARS or MERS [2].

The entity produced by this new infectious agent was named coronavirus disease 2019 (COVID-19) by WHO and declared a pandemic on March 11, 2020 [3]. By that time, the number of people infected by this new agent was close to 118,000 in 114 countries, of whom 4,291 had lost their lives to it. There are currently about 619 million cases of SARS-CoV-2 infection worldwide, with a cumulative death toll close to 6,500,000, being the United States of America the most affected country by infection and death, followed by India [4]. In our country, figures are alarming: after having surpassed four peaks since the beginning of the pandemic, there are currently 6,307,372 confirmed cases and 141,794 deaths documented [5-7].

Since the outbreak of the pandemic, a greater incidence of COVID-19 cases has been identified in men aged 34-59 years. In Colombia, the incidence of COVID-19 was 4.2% for people under 10 years, 41.5% for the group between 20 and 39 years, and 15.3% for the population over 60 years [5-7].

However, older persons and those with multiple comorbidities have a higher incidence of severe cases, primarily with pre-existing medical conditions such as cardiovascular disease, cerebrovascular disease and diabetes [8]. Thus, according to data published by the Chinese Center for Disease Control and Prevention, the overall case fatality rate of the virus was 2.3%, but among subjects aged 70 to 79 it was 8% and in those older than 80 it was 14.8%.

This can be explained by several factors associated to aging process and the presence of geriatric syndromes, such as immunosenescence (cellular, affected tissues and immune system), *inflammaging* (peripheral inflammation associated with aging and chronic diseases) favoring increased production of proinflammatory cytokines and the same SARS-CoV-2 infection [9]. Clinical manifestations of COVID-19 in the older

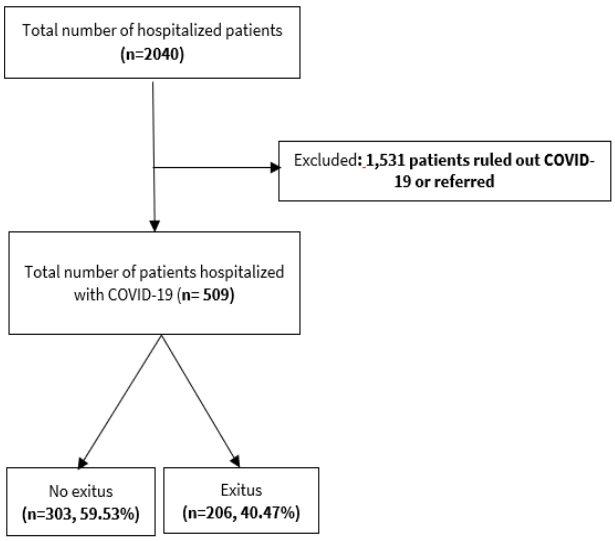

Figure 1. Flowchart of the study samples (Source: Authors' own elaboration)

adult population are varied, mainly fever followed by cough, dyspnea and rhinorrhea. Other clinical findings have been documented including general symptoms such as asthenia, anorexia, headache, diarrhea, myalgia, but at a lower rate of presentation, and even cardiovascular symptoms and complications have been described. However, the most severe involvement is pneumonia, which can be complicated by acute respiratory *distress* syndrome (ARDS) [10].

In regard to paraclinicals, observational studies have found a clear association between elevated D-dimer, lymphopenia and SOFA greater than two with increased disease progression [11]. In other Chinese cohorts, patients with higher levels of troponin I, creatinine, serum ferritin, lactate dehydrogenase and IL-6 have been shown to have a clear association with increased mortality and disease progression [12]. The aim of this study is to describe the factors associated to mortality in people over 75 years of age with confirmed COVID-19 in a high complexity hospital in the city of Bogotá, Colombia.

MATERIALS AND METHODS

Type of Study and Population

An observational, analytical and retrospective study was conducted, based on the review of medical records of a cohort of hospitalized patients under the care of a geriatrics service with a diagnosis of confirmed SARS-CoV-2, COVID-19 coronavirus infection admitted between March 1, 2020, and August 30, 2021.

The definition of confirmed SARS-CoV-2 coronavirus infection used was the positive result in high-throughput sequencing or real-time reverse transcriptase polymerase chain reaction (RT-PCR) of nasal and/or pharyngeal swab samples.

Inclusion Criteria

Patients aged 75 years or older, meeting the definition of confirmed SARS-CoV-2 coronavirus infection. Patients in this age group were included because these are the population hospitalized by the geriatric service at our institution.

Exclusion Criteria

Medical histories of patients who were referred out of the institution after admission and did not complete their care at the hospital or for whom there was no documentation of a comprehensive geriatric assessment in the records, were excluded.

Procedure

The cases were initially identified and registered in a database of all patients hospitalized by a geriatrics service in Bogotá. Patients with a confirmed diagnosis of SARS-CoV-2 infection were selected and then medical records were reviewed to verify inclusion and exclusion criteria. All data were obtained from medical records by physicians trained in comprehensive geriatric assessment and in the use of databases.

Variables

In-hospital mortality was used as the dependent variable. In the demographic variables, age was included as a continuous variable and sex as male or female.

Among clinical characteristics, symptoms at admission and time of onset were taken, reported in days since start-up.

Vital signs at the time of emergency triage assessment included respiratory rate, heart rate, systolic blood pressure, diastolic blood pressure, oxygen saturation and temperature (measured in Celsius).

For multimorbidity, a count of chronic diseases was used and was included as a continuous variable. Likewise, polypharmacy was included when there was use of five or more medications as a dichotomous variable [13].

We also took into account paraclinical findings that have previously been reported as risk factors for poor prognosis in people with COVID-19, taken in the first 48 hours after admission to the emergency department: the presence of typical radiological findings in chest images that correspond to a viral pneumonia pattern according to the radiology concept; total leukocytes taken as a continuous variable; lymphopenia defined as a peripheral blood lymphocyte count of less than 1,000 cells per milliliter [14].

The following parameters were also included: thrombocytopenia defined as a peripheral blood platelet count of less than 150,000 cells per milliliter; elevated creatinine >1.2 mg/dl; urea nitrogen (BUN) greater than 20 mg/dl; C-reactive protein (CRP) greater than 4.6; lactate dehydrogenase (LDH) greater than 350 (U/L), and positive D-dimer greater than 1000 µg/L. Gasometric parameters on admission were also included, such as arterial oxygen pressure (PaO2), arterial carbon dioxide pressure (PCO2), inspired oxygen fraction (FiO2), and arterial oxygen pressure/inspired oxygen fraction ratio (PaO2FI), making these measures continuous variables.

Sample Size Calculation

Due to the type of study and the inclusion of 100% of the confirmed cases been attended in the period of time described, it was not considered necessary to calculate the sample size. It has been established as non-probabilistic sampling. **Figure 1** shows the flowchart of the study samples.

Statistical Analysis

Categorical variables were reported as percentages and the differences between the two groups were analyzed using the Chi-square test. Quantitative variables were analyzed using the Kolmorov Smirnov statistic to determine whether they met normality criteria and are represented as mean and standard deviation (SD) if they were normally distributed variables, or as median and interquartile range (IQR) if they were non-normally distributed variables. Differences between groups for continuous variables were established using the Mann-Whitney U test. Multivariate analysis was then performed between patients who died during hospital stay and those who survived. A logistic regression model adjusted according to age and sex was constructed. Data are presented as odds ratio (OR), and a significance level of 0.05 was considered. All analyses were processed using Stata statistical software version 16.

RESULTS

Data were collected for this study from 509 patients hospitalized by the geriatrics service during the aforementioned period (**Table 1**).

Table 1. Characteristics of hospitalized population under the care of a geriatrics unit with a diagnosis of confirmed SARS-CoV-2 coronavirus infection between March 2020 & August 30, 2021

Variable	Study population (n=509)	No *exitus* (n=303, 59.53%)	*Exitus* (n=206, 40.47%)	p-value
Age, median (IQR)	83 (80-86)	82 (80-85)	83 (80-88)	0.013
Female sex, n (%)	248 (48.72%)	141 (46.53%)	107 (51.94%)	0.231
Marital status, n (%)	408	244 (59.80%)	164 (40.20%)	0.047
Single	46 (11.27%)	21 (8.61%)	25 (15.24%)	
Married	184 (45.10%)	116 (47.54%)	68 (41.46%)	
Free union	9 (2.21%)	3 (1.23%)	6 (3.66%)	
Widow(er)	148 (36.27%)	88 (36.07)	60 (36.59)	
Divorce	21 (5.15%)	16 (6.56%)	5 (3.05%)	
Educational level (years), n (%)	350	214 (61.14%)	136 (38.86%)	0.794
0	42 (12.0%)	26 (12.15%)	16 (11.77%)	
1-5	203 (58,0%)	125 (58,41%)	78 (56.36%)	
≥6	105 (29.99%)	63 (29.44%)	42 (30.88%)	
Social network				0.960
Strong social network	441 (86.81%)	264 (87.13%)	177 (86.34%)	
Social risk	57 (11.22%)	33 (10.89%)	24 (11.71%)	
Poor social network	10 (1.97%)	6 (1.98%)	4 (1.95%)	
Symptoms				
Time to symptoms, median (IQR)	7 (3-9.5)	7 (4-10)	5.5 (3-8)	0.002
Cough, n (%)	364 (71.51%)	214 (70.63%)	150 (72.82%)	0.591
Dyspnea, n (%)	289 (56.78%)	154 (50.83%)	135 (65.53%)	0.001
Fever, n (%)	229 (44.99%)	118 (38.94%)	111 (53.88%)	0.001
Myalgias, n (%)	135 (26.52%)	90 (29.70%)	45 (21.84%)	0.049
Delirium, n (%)	143 (28.09%)	64 (21.12%)	79 (38.35%)	<0.001
Diarrhea, n (%)	115 (22.59%)	75 (24.75%)	40 (19.42%)	0.159
Odynophagia, n (%)	44 (8.64%)	31 (10.23%)	13 (6.31%)	0.122
Nausea, n (%)	35 (6.88%)	18 (5.94%)	17 (8.25%)	0.312
Headache, n (%)	33 (6.50%)	25 (8.25%)	8 (3.90%)	0.051
Emesis	29 (5.70%)	15 (4.95%)	14 (6.80%)	0.378
Ageusia, n (%)	20 (3.93%)	14 (4.62%)	6 (2.91%)	0.330
Anosmia, n (%)	18 (3.54%)	10 (3.30%)	8 (3.88%)	0.727
Vital signs				
Respiratory frequency, median (IQR)	22 (19-25)	20 (18-23)	24 (20-30)	<0.001
Heart rate, median (IQR)	86 (75-98)	84 (74-95)	87.5 (75-101)	0.024
Diastolic blood pressure <60 mmHg, n (%)	95 (18.66%)	39 (12.87%)	56 (27.18%)	<0.001
Systolic blood pressure, median (IQR)	124 (108-140)	126 (110-142)	121 (107-139)	0.062
Oxygen saturation, mean (SD)	86 (80-91)	86 (82-91)	85 (76-90)	0.007
Temperature, mean (SD)	36.6 (36.2-37.1)	36.65 (36.2-37)	36.6 (36.3-37.3)	0.065
Background				
Comorbidities, median (IQR)	3 (2-4)	3 (2-4)	3 (2-4)	0.058
Arterial hypertension, n (%)	357 (70.14%)	211 (69.64)	146 (70.87)	0.765
Chronic obstructive pulmonary disease, n (%)	137 (26.92%)	75 (24.75)	62 (30.10)	0.183
Diabetes Mellitus, n (%)	134 (26.33%)	74 (24.42)	60 (29.13)	0.237
Cancer, n (%)	90 (17.68%)	39 (12.87)	51 (24.76)	0.001
Heart failure, n (%)	82 (16.11%)	52 (17.16)	30 (14.56)	0.434
Coronary heart disease, n (%)	68 (13.36%)	40 (13.20)	28 (13.59)	0.899
Chronic kidney disease, n (%)	54 (10.61%)	27 (8.91)	27 (13.11)	0.133
Stroke, n (%)	31 (6.09%)	17 (5.61)	14 (6.80)	0.584
Liver cirrhosis, n (%)	4 (0.79%)	1 (0.33)	3 (1.46)	0.158
Polypharmacy (>5 drugs), n (%)	225 (44.29%)	119 (39.40)	106 (51.46)	0.007

Table 1 (Continued). Characteristics of hospitalized population under the care of a geriatrics unit with a diagnosis of confirmed SARS-CoV-2 coronavirus infection between March 2020 & August 30, 2021

Variable	Study population (n=509)	No *exitus* (n=303, 59.53%)	*Exitus* (n=206, 40.47%)	p-value
Paraclinics				
Total leukocytes, median (IQR)	7300 (5500-10150)	6850 (5300-9200)	7950 (6100-11000)	0.001
Lymphopenia (less than 1000), n (%)	278 (54.62%)	148 (48.84%)	130 (63.11%)	0.002
Total neutrophils, median (IQR)	5550 (3800-8400)	4900 (3400-7300)	6300 (4200-9400)	0.183
Thrombocytopenia (<150,000), n (%)	114 (22.40%)	54 (17.82%)	60 (29.13%)	0.003
Lactate dehydrogenase >350(U/L), n (%)	217 (42.63%)	84 (27.72%)	133 (64.56%)	<0.001
Elevated creatinine (>1.2 mg/dl), (n%)	163 (32.02%)	77 (25.41%)	86 (41.75%)	<0.001
Elevated urea nitrogen (>20), n (%)	320 (62.87%)	166 (54.79%)	154 (74.76%)	<0.001
C-reactive protein >4.6, n (%)	397 (78%)	210 (69.31%)	187 (90.78)	<0.001
Aspartate aminotransferase, median (IQR)	31.5 (25.5-69.5)	31 (23-53)	38 (28-86)	0.864
Alanine aminotransferase, median (IQR)		27 (16-43)	27 (18-41)	0.921
Total Bilirubin, median (IQR)	0.65 (0.51-0.89)	0.65 (0.50-0.87)	0.66 (0.51-0.89)	0.294
Elevated D-dimer (>1,000 µg/L), median (IQR)	332 (65.23%)	168 (55.45%)	164 (79.61%)	<0.001
Troponin I, median (IQR)	22 (9.4-79)	15.25 (6.9-41)	47.1 (16.35-184)	0.465
pH, median (IQR)	7.44 (7.41-7.47)	7.44 (7.41-7.47)	7.44 (7.40-7.47)	0.344
PaO2, median (IQR)	68.85 (59.84.30)	71.1 (61-86.7)	64 (56.05-79.45)	<0.001
PaCO2, median (IQR)	29.03 (26-33)	30 (27-33.3)	28.4 (25-32.45)	0.029
FiO2, median (IQR)	28 (28-32)	28 (28-28)	30 (28-90%)	<0.001
PaFiO2, median (IQR)	242.5 (171-295)	264 (221-312)	90 (97-255)	<0.001
Radiological pattern				
Viral pneumonia typical changes, n (%)	386 (76.13%)	220 (72.85%)	166 (80.98%)	0.018
Viral pneumonia atypical changes, n (%)	23 (4.54%)	14 (4.64%)	9 (4.39%)	0.289
Indeterminate pattern, n (%)	32 (6.31%)	20 (6.62%)	12 (5.85%)	0.305

Note. IQR: Interquartile range; PaO2: Arterial oxygen pressure; PaCO2: Arterial carbon dioxide pressure; FiO2: Inspired fraction of oxygen; PaFiO2: Ratio of arterial oxygen pressure to inspired fraction of oxygen; & SD: Standard deviation

Among the baseline characteristics of the population, 51.28% were men and 40.47% died (p=0.013) during the hospital stay. Patients who died had a median age of 83 years (IQR=80-88, p=0.013), while patients who survived had a median age of 82 years (IQR=80-85, p=0.013). Within personal history, cancer was present in 24.76% of patients who died and in 12.87% of survivors; patients who died had a higher percentage of polypharmacy compared to survivors (51.46% and 39.4%, respectively, p=0.007).

As for clinical variables, the time of symptom presentation on admission for patients who died during hospital stay was 5.5 days (IQR 3-8), and seven days for patients who survived (IQR=4-10), p=0.002. The most frequent symptoms on admission in the *exitus* group were the presence of dyspnea in 56.78% (p=0.001); 44.99% presented fever (p=0.001) and 28.09% delirium (p<0.001).

Concerning vital signs at admission, the median respiratory rate in the group of patients who died was 24 breaths per minute (IQR=20-30) and in the survivors it was 20 (IQR=18-23), p<0.001; the median heart rate in the *exitus* group was 87.5 (IQR=75-101) and in the *non-exitus* it was 84 (IQR=74-95), p=0.024. Mean oxygen saturation was 85 in the former (SD=76-90) and in the survivors it was 86 (SD=82-91), p=0.007.

Regarding paraclinical parameters, we report the percentages of both the *exitus* and survivors groups, respectively: lymphopenia (63.11% and 48.8%, p=0.002), elevated lactate dehydrogenase (64.56% and 27.72%, p<0.001) and elevated D-dimer (79.61% vs. 55.45%, p<0.001), finding higher values in the former. Similarly, patients who died presented a higher percentage of thrombocytopenia (29.13% vs. 17.82%, p=0.003), elevated creatinine (41.75% vs. 25.41%, p<0.001), elevated urea nitrogen (74.76% vs. 54.79%, p>0.001) and higher levels of C-reactive protein (90.78% vs. 69.31%, p<0.001). For arterial blood gases level, the median arterial oxygen pressure in the group of patients who died was 64 (IQR=56.05-79.45) and in that of survivors was 71.1 (IQR=61-86.7), p<0.001; the median inspired oxygen fraction was 30 (IQR=28-90) in the deceased, and 28 (IQR:28-28) in the survivors p<0.001, and the median arterial oxygen pressure/inspired oxygen fraction ratio in the *exitus* group was 90 (IQR=97-255) and in the *non-exitus* group was 264 (IQR=221-312), p<0.001.

Furthermore, we found that the percentage of deceased patients with radiological findings typical of viral pneumonia was 80.98% while that of surviving patients was 72.8%, p=0.018. The remaining baseline characteristics of the patients are shown in **Table 1**.

After performing a multivariate logistic regression analysis for in-hospital mortality due to SARS-CoV-2 infection, adjusted according to age and sex (**Table 2**), it was found that a shorter time to onset of symptoms on admission (OR=0.95, 95% CI=0.91-0.99, p=0.034), a respiratory rate greater than 20 breaths per minute (OR=1.91, 95% CI=1.16-3.13, p=0.010), having thrombocytopenia (OR=2.41, 95% CI=1.35-4.31, p=0.003), elevated lactate dehydrogenase (OR=2.01, 95% CI=.19-3.39, p=0.009) and elevated D-dimer (OR=2.47, 95% CI=1.49-4.10, p=0.000) are associated to a higher in-hospital mortality from SARS-CoV-2 infection.

DISCUSSION

COVID-19 infection has a high prevalence and complications in older adults. The present study evaluated the factors associated with mortality due to COVID-19 infection in an older adult population over 75 years of age in a hospital in Bogotá, Colombia, finding correlation with other studies previously published in similar samples.

Mortality during hospital stay was 40.47%. One of the factors associated with higher mortality was age, so that the older the person was, the greater the probability of death.

Table 2. Regression model of mortality, symptoms, vital signs, history, and paraclinicals

Variable	Unadjusted analysis OR (95%CI)	p	Adjusted analysis* OR (95%CI)	p
Symptom time, days	0.94 (0.91-0.98)	0.002	0.95 (0.91-0.99)	0.034
Dyspnea	1.83 (1.27-2.65)	0.001	1.19 (0.72-1.93)	0.482
Fever	1.83 (1.20-2.62)	0.001	1.46 (0.90-2.39)	0.124
Delirium	2.32 (1.56-3.44)	0.000	1.46 (0.87-2.44)	0.143
Respiratory rate >20	3.03 (2.08-4.41)	<0.001	1.91 (1.16-3.13)	0.010
Heart rate	1.01 (1.002-1.02)	0.012	1.00 (0.98-1.01)	0.729
Diastolic blood pressure <60 mmHg	2.52 (1.60-3.98)	<0.001	1.78 (0.98-3.22)	0.055
Oxygen saturation	0.95 (0.94-0.97)	<0.001	0.99 (0.97-1.02)	0.897
Temperature	1.25 (1.00-1.57)	0.045	1.21 (0.88-2.25)	0.220
Polypharmacy (>5 drugs)	1.63 (1.13-2.33)	0.007	1.41 (0.88-2.25)	0.146
Cancer	2.22 (1.40-3.53)	0.001	2.27 (1.25-4.11)	0.007
Total leukocytes	1.00 (1.00002-1.0001)	0.002	1.00 (0.99-1.00)	0.501
Thrombocytopenia (<150,000)	1.89 (1.24-2.88)	0.003	2.41 (1.35-4.31)	0.003
Lactate dehydrogenase >350	4.75 (3.24-6.94)	0.000	2.01 (1.19-3.39)	0.009
Creatinine	1.33 (1.07-1.66)	0.009	0.99 (0.77-1.29)	0.994
Elevated urea nitrogen (>20)	2.44 (1.65-3.60)	0.000	1.14 (0.66-1.97)	0.623
C Reactive Protein >4.6	4.35 (2.56-7.41)	0.000	1.58 (0.82-3.03)	0.164
Elevated D-dimer (>1000 µg/L)	3.13 (2.08-4.71)	0.000	2.47 (1.49-4.10)	0.000
PaO2	0.98 (0.97-0.99)	0.000	0.99 (0.98-1.01)	0.773
PaFiO2	0.99 (0.98-0.99)	0.000	0.99 (0.99-0.99)	0.001

Note. *Age and gender adjusted; OR: Odds ratio; CI: Confidence interval; PaO2: Arterial oxygen pressure; & PaFiO2: Arterial oxygen pressure/inspired oxygen fraction ratio

Similar data have been found in several studies in which age plays a fundamental role. Thus, in a study published by Wu et al., with data from 72,314 cases in China, it was found that mortality increased significantly with age, with a case fatality rate of 8% in patients aged between 70 and 79, and 14.8% for patients over 80 years [15]. Similarly, a Spanish study carried out in patients older than 75, reports a mortality rate similar to ours with 47.6%, but when divided into two groups, 75 to 84, and over 85 years, a higher mortality was found in the very old group [16].

In the present study, a significant association was found between a shorter time of symptom onset at hospital admission and mortality, as well as a clear one between dyspnea (65.3%), fever (53.8%) and delirium (38.5%), and a higher risk for mortality. Similar findings in other studies, such as that of Azwar et al., a research in Indonesia in which 60% of the patients who died had fever and 60% had dyspnea, showed that this did not have a statistically significant value in relation to mortality [17]. Similarly, in the study by Zhou et al. 63% of the deceased were found to have dyspnea on admission; however, although 94% of the patients who died had fever, this was not statistically significant. In our study, 60% of the patients who died had fever, but it is important to remember the low systemic inflammatory response in older adults and fever is usually attenuated or absent and can delay the diagnosis, so it should not be considered as a cardinal sign for the diagnosis of COVID-19 [18].

Also, in our study, the presence of delirium was associated with higher mortality. In a meta-analysis by Shao et al., a review of 48 studies, it was found that the presence of delirium represented a mortality rate three times higher in patients with COVID-19 infection [19]. In another study published in Brazil, it was reported that delirium was associated with 55% of in-hospital mortality in older adults with COVID-19 infection; it was also associated with a longer hospital stay, longer admission to the intensive care unit and use of mechanical ventilation [20]. Delirium is a manifestation of multiple diseases and predisposing factors, mainly age and dementia, which increases the risk of mortality in the presence of any other pathology [21]. In general, delirium is an expression of higher biological vulnerability with increased severity of the disease, so it deserves a thorough clinical evaluation to identify conditions that are likely to intervene to prevent its occurrence, as well as to identify those acute medical situations that require treatment and that can lead the patient to death. Therefore, the diagnosis and management of delirium should always accompany the approach to an older adult with COVID-19.

The data obtained in this study showed an association between the presence of oncologic pathology (24.7%) and higher mortality due to COVID-19. In 2020, Parohan et al. published a meta-analysis finding a clear relationship between having a history of cancer and mortality. However, unlike our study, they found a greater connection with other entities such as hypertension, cardiovascular disease, chronic obstructive pulmonary disease and diabetes, and higher mortality [22].

Likewise, a meta-analysis published in 2021 that included 42 studies found that having cancer was associated with worse outcomes, as was having comorbidities such as chronic obstructive pulmonary disease, diabetes, hypertension, chronic kidney disease, cardiovascular disease, among others, as well as obesity and active smoking, and being male [23].

Other factors associated with mortality found in our study were higher respiratory (24, IQR=20-30) and heart rates (87.5, IQR=75-101). Similarly, 27.1% of the deceased patients had a diastolic pressure lower than 60 mmHg, as well as lower oxygen saturation at admission (85, SD=76-90). A Spanish study evaluating predictors of mortality due to COVID-19 found that, in addition to age, inflammatory markers and symptoms such as dyspnea and delirium, and oxygen saturation on admission lower than 90% had a significant association with higher mortality during hospital stay [24].

These findings are related to the clinical characteristics of the virus, which include a greater predilection for aerial tract involvement, generating pulmonary infiltrates with dyspnea and hypoxemia, resulting in greater severity of the symptoms [25].

However, at laboratory results stage, in the present study statistically significant values were found between elevated lactate dehydrogenase >350 (U/L), presence of elevated D-dimer greater than 1,000 µg/L, as well as a Pa02/Fi02 ratio with a median less than 90. These findings correlate with the world literature where the presence of these elevated markers has been reported with increased mortality. In a study published by Tang et al., it was shown how elevated D-dimer values had a clear association with mortality, due to the increased thrombotic risk produced by the disease [26].

Although in our study parameters such as coagulation times or fibrinogen were not measured, in cases of severe infection a state of increased procoagulability has been documented, which on some occasions is related to disseminated intravascular coagulation, derived from sepsis and multiorgan dysfunction caused by infection from the SARS-CoV-2 virus [27]. For this reason, the current recommendations of the International Society on Thrombosis and Hemostasis and other scientific societies recommend initiating thromboprophylaxis in all patients with COVID-19 requiring hospitalization, since it has been shown to reduce mortality due to COVID-19 during hospital stay [28-30].

Similarly, in a meta-analysis published by Henry et al., they found an association between elevated LDH levels with a six-fold increased likelihood of severe disease and a 16-fold increased risk of mortality, so that LDH measurement in patients with COVID-19 infection on admission should be taken as a measure for risk stratification [31]. This partly explains why LDH is commonly used for measurement of tissue damage, including in lung diseases due to the elevated presence of its isoenzyme three. During pulmonary injury situations such as interstitial lung disease, as well as in viral events such as SARS-CoV-2 pneumonia, there is a marked increase in LDH as a process of lung tissue damage. In addition, LDH is elevated in the presence of thrombotic microangiopathy, characteristic of COVID-19 infection, associated to renal failure and myocardial lesion [32].

Knowing the natural history of this new entity in the elderly it help us to generate hypothesis and identify possible diagnostic, prognostic and treatmet alternatives that must be confirmed in further studies.

In our study we found several strengths: first, the evaluations and management were performed in a highly complex hospital, which allowed for the availability of diagnostic tests and permanent follow-up. Second, the standardization of the approach, diagnosis and management was based on institutional and national guidelines, which were updated and modified, as new aspects of the disease became known. Third, there are few studies in Latin America with such a large sample of adult patients over 75 years of age with COVID-19 as ours.

However, it is important to mention some limitations of our study. Being a retrospective analysis, the data were obtained from electronic medical records of a hospital. Additionally, not all patients diagnosed with SARS-CoV-2 infection were included, and this could result in a reduced sample, but it should be noted that the information obtained is reliable and the patients were included long after their outcome was known. Moreover, there was no short or medium-term follow-up of patients discharged from our service after hospitalization for COVID-19. Future studies should focus on expanding the population to determine the impact of medium and long-term complications, as well as mortality after hospital stay.

CONCLUSIONS

When evaluating the factors associated to mortality in persons older than 75 years with confirmed COVID-19, admitted to a high complexity hospital, we found similarity with what has been previously published, highlighting that there is a significant association between mortality and a shorter time of symptoms onset at admission, in addition to the presence of dyspnea, fever and delirium. In the analysis of paraclinics, the elevation of lactate dehydrogenase >350, the presence of elevated D-dimer greater than 1,000 µg/L, as well as a Pa02/Fi02 ratio with a median of less than 90, confirm this association with higher mortality.

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