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Factors Associated with Mortality in Patients with COVID-19 from a Hospital in Northern Peru

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Abstract: We aimed to identify the factors associated with mortality in patients with COVID-19 from the hospitalization service of the Cayetano Heredia Hospital, Piura, Peru, from May to June 2020. A prospective study was conducted in hospitalized patients with a confirmed diagnosis of COVID-19 through serological and/or molecular reactive testing. The dependent variable was death due to COVID-19, and the independent variables were the epidemiological, clinical and laboratory characteristics of the patient. The chi-square test and the non-parametric Mann–Whitney U test were used, with a significance level of 5%. Of 301 patients with COVID-19, the majority of them were male (66.1%), and the mean age was 58.63 years. Of the patients analyzed, 41.3% of them died, 40.2% of them were obese and 59.8% of them had hepatic steatosis. The three most frequent signs/symptoms were dyspnea (90.03%), fatigue (90.03%) and a cough (84.72%). Being an older adult ($p = 0.011$), being hospitalized in the ICU ($p = 0.001$), overweight ($p = 0.016$), obese ($p = 0.021$) and having compromised consciousness ($p = 0.039$) and thrombocytopenia ($p = 0.024$) were associated with mortality due to COVID-19. Overall, the mortality rate due to COVID-19 was 41.3%. Having an older age, being hospitalized in the ICU, overweight, obese and having compromised consciousness and thrombocytopenia were positively associated with mortality in patients with COVID-19. These findings highlight the need to establish an adequate system of surveillance and epidemiological education in hospitals and communities in the event of new outbreaks, especially in rural and northern Peru.

Keywords: COVID-19; coronavirus infections; mortality; prospective studies; Peru; death

1. Introduction

In December 2019, the first cases of COVID-19 were reported in the city of Wuhan-China [1]. Peru is one of the countries with the highest mortality estimates during the

pandemic period [2,3]. Although social distancing and quarantine (measures related with a significant reduction of COVID-19 incidence [4]) were implemented in this country, the frequency of deaths [2] and mental distress [5] were substantially high. Peru has a fragile healthcare system, which is aggravated by limited organizational support in healthcare facilities [3,6]. Furthermore, technostress related to mental distress [7] became evident, and the population implemented self-care behaviors such as the use of medicinal plants [8] in a country that consumes multiple plants for medicinal purposes based on their bioactive substances content [9,10].

Studies have determined that the male sex, older age [11], and presenting diabetes, hypertension and chronic kidney disease are associated with a greater severity of illness and mortality from COVID-19 [12,13]. In Peru, among the patients with COVID-19 who were admitted to a public hospital in Peru, the in-hospital mortality rate was high, and it was independently associated with oxygen saturation below 90% on admission and with an age of over 60 years [14]. Additionally, the patients with a history of hypertension, diabetes mellitus and obesity were also associated with a higher risk of mortality due to COVID-19 [14,15]. Regardless of these reported mortality risk factors, the vaccination intention in Peru has been reported to be affected by the education level, being a healthcare worker and if they had a previous COVID-19 infection [16].

There have been several systematic reviews and meta-analyses on the factors associated with mortality related to COVID-19. Among them, it has been shown that demographic, patient history, physical examination, laboratory and radiological factors, as well as a high SOFA score contribute importantly to deaths [17,18]. There are major predictors such as comorbidities, in which diabetes has a major contribution to deaths [19], but also, obesity, hypertension, cardiovascular disease, cancer and age has important influence on fatal outcomes [20]. There has also been research on specific populations, for example, deaths among older people have been related to dementia, diabetes, chronic kidney disease and hypertension [21]. There are even systematic reviews on specific regions of the world, remarking on their proper risk factors such as in Europe (88 cohort studies, 6,653,207 patients, risk factors: solid organ tumors, diabetes, renal disease, arrhythmia, ischemic heart disease and liver disease) [22] and sub-Saharan Africa (12 studies, 43,598 patients, mortality 4.8%, risk factors: advanced age, male sex, chronic kidney disease, hypertension, severe or critical condition on admission, a cough and dyspnea) [23].

However, there are a paucity of published studies and data from Latin America examining COVID-19 mortality [24,25]. The previous literature in this region has not addressed the presence of hepatic steatosis, dyslipidemia, impaired consciousness and other clinical biochemical markers as prognostic risk factors for COVID-19 mortality. Therefore, this current research aims to further document and understand the potential clinical factors associated with a high mortality rate in Peru. This study serves as a basis to obtain a broader vision of the impact of the pandemic in Peru and other developing nations and propose changes in the management or investment of resources based on this experience and findings. For all of the above, this research aims to determine and categorize the factors associated with mortality in hospitalized Peruvian patients in northern Peru by analyzing the demographic characteristics, comorbidities, evolution and laboratory parameters of the patients with an SARS-CoV-2 infection.

2. Methodology

2.1. Study Design, Population and Sample

A prospective analytical study was carried out on patients hospitalized in COVID-19 areas of the Cayetano Heredia Hospital (hospitalization service and adult intensive care unit). It included patients who were older than 18 years with clinical suspicion of COVID-19 (defined according to the technical standard of the Ministry of Health [26]), which was confirmed by at least one reactive test of serological type (immunochromatography, immunochemiluminescence) and a molecular one (qRT-PCR). The patients who had incomplete clinical or laboratory information were excluded from the analysis of this research ($n = 15$).

Using these criteria and a convenience sampling method, a sample of 301 patients were considered for the analysis.

2.2. Study Procedures

We collected the clinical and epidemiological data from patients hospitalized both on the medical floor and in critical areas of the ICU due to COVID-19 at the Cayetano Heredia Hospital in Piura during the period of May-June 2020. The data collection sheet was used in the hospitalization of the COVID-19 patient until their discharge or death. The information was entered into a database designed in the Microsoft Excel 2016 program. Authorization was requested from Hospital Cayetano Heredia after the study was approved by the ethics committee.

2.3. Instruments and Variables

The data collection form consisted of general, clinical and laboratory data. In the general section, their sex, age, hospitalization service, evolution and number of days of hospitalization were examined. The clinical section collected information on body mass index and comorbidities (diabetes, hypertension, dyslipidemia, heart disease, smoking, HBV-HCV, hepatic steatosis, gastroesophageal reflux disease, peptic ulcer, cirrhosis, cancer, chronic kidney disease and pulmonary tuberculosis), while in the laboratory section, the presence of altered findings of TGO/TGP (>37 U/L/ >41 U/L), albumin (<3.5 g/dL), INR (>1.2), alkaline phosphatase (>147 U/L), GGT (>40 U/L) and platelets ($<125 \times 10^9$ /L) were tabulated. The dependent variable was mortality due to a COVID-19 infection, which was operationally defined as the finding of death in the clinical records of patients hospitalized in the COVID-19 area of the Cayetano Heredia-Piura hospital. The independent variables were the general, clinical and laboratory characteristics that have previously been detailed.

2.4. Statistic Analysis

The statistical analysis was performed using Stata 15.0. Previously, less than 20% of the sampled population verified the potential loss of observations. The descriptive analysis reported absolute and relative frequencies for the categorical variables. The best measure of central tendency and dispersion in the numerical variables was estimated. The factors associated with mortality were investigated in a bivariate analysis using the chi-square test and the non-parametric Mann-Whitney U test. A significance level of 5% was used. The simple and multiple regression analysis estimated the risk ratios (RR) and 95% confidence intervals. Generalized linear models, Poisson distribution family, robust variance and a log link function were employed. Only the variables that reached statistical significance ($p < 0.005$) in the simple regression model were included in the multiple regression model. The collinearity between the variables of interest was evaluated.

2.5. Ethical Considerations

The study received authorization from the Institutional Research Ethics Committee of Hospital Cayetano Heredia (Piura). The bioethical principles stipulated in the Taipei Declaration were respected. Patient confidentiality was maintained using anonymized codes in the database.

3. Results

Of 301 patients with COVID-19 selected for this investigation, it was found that the majority of them were male (66.1%) and belonged to the group of older adults (52.8%). Some of them were hospitalized in the ICU (11.3%), and the median hospital stay was 9 days (2–55 days). Some of them were obese (40.2%), and most of them had the following comorbidities: hepatic steatosis (59.8%), dyslipidemia (40.5%), hypertension (39.2%) and diabetes (23.3%). More than half of them presented abnormalities in the albumin tests (82.2%), GGT (51.4%), TGP (49.5%) and TGO (46.1%). Some of the patients died (41.3%) (Table 1).

Table 1. Characteristics of patients with COVID-19 treated at the Cayetano Heredia Hospital, Piura, Peru.

Characteristics	N (%)
Sex	
Female	102 (33.9)
Male	199 (66.1)
Age (years) *	58.63 ± 16.44
Age (categorized)	
Teen/Young adult (18–29)	14 (4.7)
Adult (30–59)	128 (42.5)
Elderly (60+)	159 (52.8)
Service	
Hospitalization	267 (88.7)
ICU	34 (11.3)
Days of hospitalization **	9 (2–55)
BMI (categorized)	
Normal	79 (26.3)
Overweight	101 (33.6)
Obesity	121 (40.2)
Comorbidities	
Diabetes	70 (23.3)
Hypertension	118 (39.2)
Dyslipidemia	122 (40.5)
Ischemic heart disease	12 (4.0)
Tobacco use (Smoker)	20 (6.6)
HBV-HCV	4 (1.3)
Hepatic steatosis	180 (59.8)
Gastroesophageal reflux disease	6 (2.0)
Peptic ulcer	2 (0.7)
Cirrhosis	4 (1.3)
Cancer	14 (4.7)
Pregnancy	14 (4.7)
Chronic kidney disease	20 (6.6)
Tuberculosis	1 (0.3)
Altered laboratory findings	
TGO (U/L) †	130 (46.1)
TGP (U/L) †	140 (49.5)
Albumin (g/dL) †	83 (82.2)
INR †	34 (12.1)
Alkaline phosphatase (U/L) †	64 (26.7)
GGT (U/L) †	37 (51.4)
Platelets ($\times 10^3/\text{mm}^3$)	28 (9.3)
Clinical Evolution †	
Discharge	176 (58.7)
Died	124 (41.3)

* Mean ± Standard deviation; ** Median (minimum value–maximum value); † Some values do not contribute to the 301 patients due to unavailable data.

The most frequent signs/symptoms in COVID-19 patients were dyspnea (90.03%), fatigue (90.03%), a cough (84.72%) and a fever (72.43%) (Figure 1).

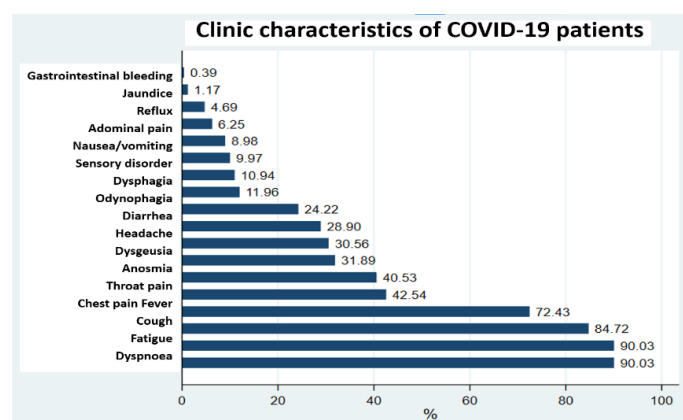


Figure 1. Clinical characteristics of COVID-19 patients.

In the bivariate analysis, it was determined that in older adults, there was a 23.1% higher frequency of death compared to that of the rest of the young adult population (52.2% vs. 29.1%; $p < 0.001$). Those patients admitted to the ICU had a 36.3% higher frequency of fatal outcomes compared to that of the patients hospitalized in the general medical ward (73.5% vs. 37.2%; $p < 0.001$). Additionally, the three most frequent symptoms that were associated with mortality were impaired consciousness, dyspnea and fatigue ($p < 0.05$) (Table 2).

Table 2. Factors associated with mortality in patients with COVID-19 treated at the Cayetano Heredia Hospital, Piura, Peru, in a bivariate analysis.

Variables	Evolution		p-Value *
	Discharge (n = 176) n (%)	Died (n = 124) n (%)	
Sex			0.127
Female	66 (64.7)	36 (35.3)	
Male	110 (55.6)	88 (44.44)	
Elderly >60 years			<0.001
No	100 (70.9)	41 (29.1)	
Yes	76 (47.8)	83 (52.2)	
Medical Ward Service			<0.001
Hospitalization	167 (62.8)	99 (37.2)	
ICU	9 (26.5)	25 (73.5)	
Days of Hospitalization **¶	9 (2–48)	10 (2–55)	0.188
BMI (categorized)			0.064
Normal	54 (68.4)	25 (31.7)	
Overweight	60 (59.4)	41 (40.6)	
Obesity	62 (51.7)	58 (48.3)	
Comorbidities †			
Diabetes	38 (54.3)	32 (45.7)	0.395
Hypertension	61 (51.7)	57 (48.3)	0.048
Dyslipidemia	64 (52.9)	57 (47.1)	0.095

Table 2. Cont.

Variables	Evolution		<i>p</i> -Value *
	Discharge (<i>n</i> = 176)	Died (<i>n</i> = 124)	
	<i>n</i> (%)	<i>n</i> (%)	
Ischemic heart disease	6 (50.0)	6 (50.0)	0.540
Tobacco use (Smoker)	11 (57.9)	8 (42.1)	0.944
HBV-HCV	1 (25.0)	3 (75.0)	0.169
Hepatic steatosis	99 (55.3)	80 (44.7)	0.151
Gastroesophageal reflux disease	5 (83.3)	1 (16.7)	0.215
Cirrhosis	3 (75.0)	1 (25.0)	0.504
Cancer	6 (54.6)	5 (45.5)	0.777
Pregnancy	13 (92.9)	1 (7.1)	0.008
Chronic kidney disease	8 (40.0)	12 (60.0)	0.079
Clinical Symptomology †			
Fever	130 (59.9)	87 (40.1)	0.480
Throat pain	77 (63.6)	44 (36.4)	0.151
Odynophagia	22 (61.1)	14 (38.9)	0.751
Cough	145 (57.1)	109 (42.9)	0.192
Chest pain	36 (63.2)	21 (36.8)	0.193
Headache	63 (72.4)	24 (27.6)	0.002
Fatigue	154 (57.0)	116 (43.0)	0.086
Anosmia	65 (67.7)	31 (32.3)	0.029
Dyspnea	150 (55.6)	120 (44.4)	0.001
Commitment of conscience	10 (33.3)	20 (66.7)	0.003
Dysgeusia	61 (66.3)	31 (33.7)	0.074
Nausea/vomiting	16 (69.6)	7 (30.4)	0.431
Reflux	7 (58.3)	5 (41.7)	0.791
Dysphagia	19 (67.9)	9 (32.1)	0.496
Abdominal pain	10 (62.5)	6 (37.5)	0.963
Diarrhea	48 (77.4)	14 (22.6)	0.004
Altered laboratory findings †			
TGO (U/L) †	76 (58.5)	54 (41.5)	0.714
TGP (U/L) †	86 (61.9)	53 (38.1)	0.110
Albumin (g/dL) †	52 (62.7)	31 (37.4)	0.320
INR †	20 (58.8)	14 (41.2)	0.939
Alkaline phosphatase (U/L) †	35 (54.7)	29 (45.3)	0.919
GGT (U/L) †	24 (64.9)	13 (35.1)	0.550
Platelet ($\times 10^3/\text{mm}^3$)	11 (39.3)	17 (60.7)	0.029

* *p*-values calculated with the Chi-Square test of independence; ** *p*-value calculated with the Mann–Whitney U test; † Median (minimum value–maximum value); ‡ Absolute and relative frequencies of the categories of interest are shown (Yes); † Some values do not contribute to the 301 patients due to unavailable data.

In the simple regression analysis, we observed that the risk factors for mortality due to COVID-19 were being an older adult (RR = 1.80), having been hospitalized in the ICU (RR = 1.98), being obese (RR= 1.53), and having a history of hypertension (RR = 1.31), HBV-HCV (RR = 1.83) and CKD (RR = 1.50). Regarding the clinical laboratory findings, it was delineated that having dyspnea (RR = 3.33), impaired consciousness (RR = 1.73) and thrombocytopenia (RR = 1.54) were risk factors for mortality due to an infection by SARS-CoV-2. On the contrary, a headache (RR = 0.59), anosmia (RR = 0.71) and diarrhea (RR = 0.53) were found to be potential protective factors for death (Table 3).

Table 3. Risk factors for mortality due to COVID-19 in patients treated at the Cayetano Heredia hospital, Piura, Peru, in simple and multiple regression analyses.

Characteristics	Simple Regression			Multiple Regression		
	RR	IC 95%	<i>p</i> -Value *	RR	IC 95%	<i>p</i> -Value *
Sex						
Female	Ref.					
Male	1.26	0.93–1.71	0.140			
Elderly						
No	Ref.			Ref.		
Yes	1.80	1.33–2.42	<0.001	1.69	1.13–2.53	0.011
Service						
Hospitalization	Ref.			Ref.		
ICU	1.98	1.53–2.55	<0.001	2.29	1.40–3.75	0.001
Days of hospitalization **	1.01	1.00–1.02	0.169			
BMI (categorized)						
Normal	Ref.			Ref.		
Overweight	1.28	0.86–1.92	0.224	1.68	1.10–2.55	0.016
Obesity	1.53	1.06–2.22	0.026	1.64	1.08–2.49	0.021
Comorbidities **						
Diabetes	1.14	0.85–1.54	0.384			
Hypertension	1.31	1.00–1.71	0.046	1.09	0.81–1.48	0.572
Dyslipidemia	1.26	0.96–1.65	0.092			
Heart disease	1.22	0.68–2.18	0.511			
Tobacco use (smoker)	1.02	0.59–1.76	0.943			
HBV-HCV	1.83	1.02–3.29	0.041	1.84	1.16–2.92	0.010
Hepatic steatosis	1.23	0.92–1.64	0.159			
Gastroesophageal reflux disease	0.40	0.07–2.40	0.316			
Cirrhosis	0.60	0.10–3.31	0.559			
Cancer	1.10	0.57–2.14	0.770			
Pregnancy	0.17	0.02–1.11	0.064			
Chronic kidney disease	1.50	1.02–2.21	0.040	1.29	0.85–1.96	0.238

Table 3. Cont.

Characteristics	Simple Regression			Multiple Regression		
	RR	IC 95%	<i>p</i> -Value *	RR	IC 95%	<i>p</i> -Value *
Clinic **						
Fever	0.90	0.67–1.20	0.474			
Throat pain	0.82	0.61–1.08	0.159			
Odynophagia	0.93	0.60–1.44	0.756			
Cough	1.32	0.85–2.04	0.221			
Chest pain	1.40	0.84–2.33	0.195			
Headache	0.59	0.41–0.85	0.005	0.87	0.59–1.28	0.483
Fatigue	1.61	0.88–2.97	0.126			
Anosmia	0.71	0.51–0.98	0.039	1.03	0.71–1.49	0.875
Dyspnea	3.33	1.32–8.39	0.011	2.33	0.77–7.05	0.133
Commitment of conscience	1.73	1.29–2.32	<0.001	1.54	1.02–2.33	0.039
Dysgeusia	0.75	0.54–1.04	0.088			
Nausea/vomiting	0.78	0.41–1.49	0.457			
Reflux	1.10	0.55–2.19	0.785			
Dysphagia	0.83	0.47–1.46	0.515			
Abdominal pain	0.98	0.51–1.89	0.964			
Diarrhea	0.53	0.32–0.86	0.010	0.64	0.39–1.03	0.067
Altered laboratory findings **						
TGO (U/L)	0.95	0.72–1.25	0.715			
TGP (U/L)	0.80	0.61–1.05	0.113			
Albumin (g/dL)	0.75	0.43–1.28	0.292			
INR	0.98	0.64–1.51	0.939			
Alkaline phosphatase (U/L)	1.02	0.74–1.40	0.919			
GGT (U/L)	1.23	0.62–2.45	0.555			
Platelets ($\times 10^3/\text{mm}^3$)	1.54	1.11–2.15	0.011	1.57	1.06–2.32	0.024

* *p*-values obtained with Generalized Linear Models (GLM), Poisson family, log link function and robust variance;

** RR of categories of interest are shown (Yes).

In the multiple regression, the associations found in the simple regression were partially maintained. The patients who were older than 60 years and had been hospitalized in the ICU were risk factors for dying from COVID-19. Overweight patients, obesity, impaired consciousness and thrombocytopenia presented 68% (RR = 1.68), 64% (RR = 1.64), 54% (RR = 1.54) and 57% (RR = 1.57) increased risks of mortality due to an SARS-CoV-2 infection, respectively (Table 3 and Figure 2).

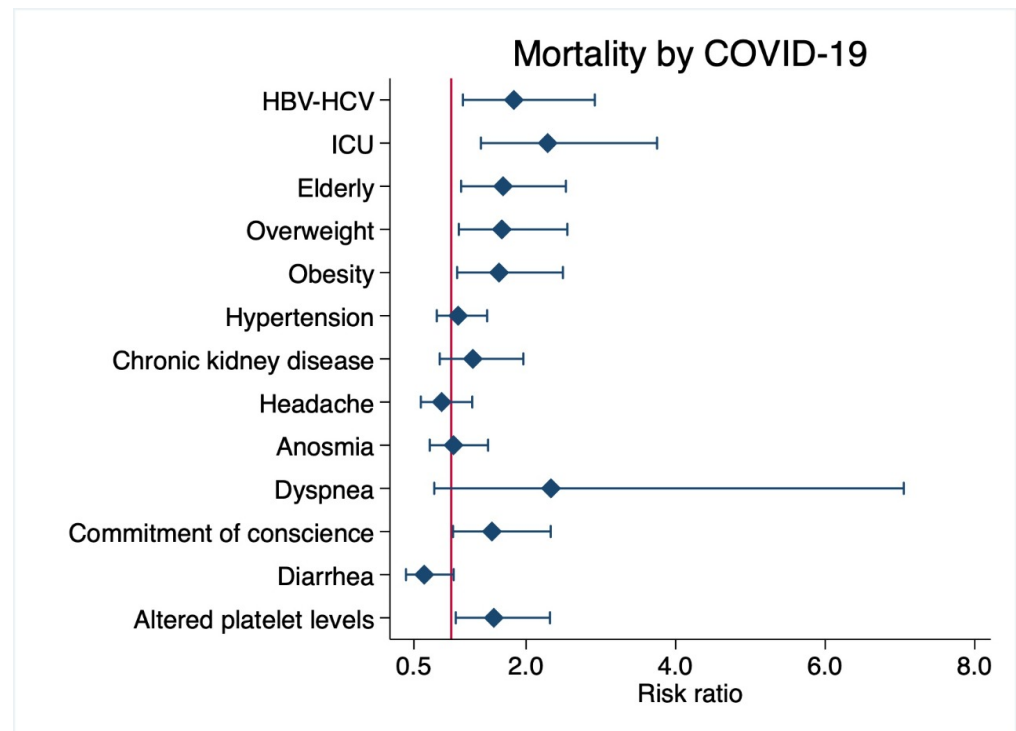


Figure 2. Forest plot of the risk factors for mortality due to COVID-19.

4. Discussion

The analysis of the collected data determined that the mortality from COVID-19 was 41.3% of the patients studied. Hepatic steatosis, dyslipidemia, hypertension and diabetes were the most frequent comorbidities in the study subjects who were evaluated. The abnormal clinical biochemical biomarkers in more than half of the patients included reduced albumin and elevated GGT levels. Most of the patients presented clinical characteristics of dyspnea, fatigue, a cough and a fever. The factors associated with a higher risk of dying due to an SARS-CoV-2 infection were being an older adult, having been hospitalized in the ICU, being overweight, obese, having an impaired consciousness and thrombocytopenia. The lethality rate from COVID-19 in our study was 41.3%, which parallels and is similar to a seminal investigation that was carried out in New York City, in which 43% of patients died from an SARS-CoV-2 infection [27]. However, it contrasts and is a higher than those which were reported by Li et al. (9.4%) [28] and Fumagalli et al. (23.2%) [29]. At the regional and local levels, our findings represents one of the highest fatality rates reported in the literature, and it is in contrast to what has been estimated in Puebla, Mexico (35%), Santiago, Chile (27.4%), and Lima, Peru (29.4%) [30–32]. Peru had 194,935 deaths in 2020 from COVID-19, which ranked in the first place for mortality per million inhabitants at the regional and global levels [33].

The high mortality found in this research could be due in part to the insufficient amount of human and material resources available for hospital care, such as the low availability of oxygen, intensive care unit (ICU) beds (two ICU beds per hundred thousand inhabitants) and lack of personal protective equipment (PPE) and molecular tests [34–36]. In addition, since this hospital was designated and intended exclusively for the care of COVID-19 patients in the Piura region during the health emergency period of the pandemic, the clinical condition of the admitted patients was unfavorable.

Our results indicated that being an older adult (over 60 years of age) increases the risk of dying from COVID-19 by 69%, which is consistent with previously reported findings in other studies [37–39]. However, it differs from other studies which indicate that the risk of dying from COVID-19 is not significantly associated with age [40]. The vulnerability of our patients could explain this association to COVID-19, which is strictly dependent

on biological age and related to other age-related diseases, which is characterized by the hyperfunction response of inflammatory cells to an infection, which can trigger cytokine storm hypercoagulation, lung and distant organ damage [41].

Being hospitalized in the ICU represented a 129% higher risk of dying from COVID-19. This finding parallels that described by some studies with high mortality rates [42–45]. A meta-analysis reported that the mortality rate in patients admitted to the ICU and with mechanical ventilation had a range of 15–78%. A possible explanation is the scarce rationing of resources in saturated ICUs, the lack of an adequate number of ICU beds and an insufficient response capacity [46,47]. In addition, some clinical features that have been identified more frequently in patients who had a fatal outcome include dyspnea, lower initial oxygen saturation and a lower lymphocyte count were observed in patients with late diagnosis and management [48]. Likewise, late mechanical ventilation is associated with the deterioration of patients in the ICU since the use of a ventilator can have serious consequences such as a lung injury, respiratory infections, alterations in venous return, formation of deep vein thrombosis and pulmonary thromboembolism, which can increase the risk of mortality [49–51].

Being overweight and obese were determined to be risk factors for mortality from COVID-19 in our study. The potential biological mechanisms that would explain this relationship are the hormonal, anti-inflammatory and pro-inflammatory imbalances of adiponectin due to the excess of dysfunctional adipose tissue, which may interfere with the activation of the immune system, and consequently, these can generate a poor immune response [48]. The high concentrations of proinflammatory cytokines that are produced in the adipose tissue (mainly in men) and the induction of a “cytokine storm” could be possible causes of respiratory failure in the most severe forms of COVID-19, which translates into a worse prognosis [48–50].

The patients who presented compromised consciousness had a 54% higher risk of mortality from COVID-19. This is consistent with the findings of Lee et al. who found that having altered mental status increased the risk of dying by 5.4 times [52]. The potential explanation for this association is due to the invasion of the brainstem by the virus through the angiotensin-converting enzyme 2 receptors, which facilitates the alteration at the level of the ascending reticular activation system (SARA) [53].

The presence of thrombocytopenia is associated with a 57% increased risk of death from COVID-19. An investigation found that having a platelet count of $<125 \times 10^9/L$ can increase the probability of death from COVID-19 by 60% [25]. This finding contrasts with what which was described by Zhou et al. [40], who did not show an association between the number of platelets and death from COVID-19, which could be due to an advance in the severity of the disease due to increased lung tissue damage, causing platelet activation and aggregation, leading to the formation of thrombi that lead to platelet consumption.

Our research has limitations such as collecting data from a single care center and a small number of patients compared to larger metropolitan studies. Therefore, it has potential selection bias. In addition, the measurement bias was not possible to evaluate as well as the collection of some relevant variables due to the high workload of the first-line human resources who collected the data during the first pandemic wave. Therefore, other clinical variables such as oxygen saturation, the respiratory rate on admission, qSOFA score and other biochemical parameters such as D-dimer, creatinine, CRP and troponin I could be considered in future studies. However, to our knowledge, this study is one of the first Peruvian studies that has evaluated the association between COVID-19 mortality with the sociodemographic, clinical and laboratory factors in northern Peruvian cities such as Iquitos, Lambayeque and Trujillo, which have been greatly affected by COVID-19.

5. Conclusions

In conclusion, the mortality rate from COVID-19 was 41.3% among the hospitalized patients during the early first pandemic wave in Peru. In addition, being of an older

age, admitted to the ICU, overweight, obese, and having an impaired consciousness and thrombocytopenia were associated with mortality in patients with COVID-19.

The findings of this research and analysis are relevant because the rapid transmission and high fatality rate of COVID-19 require us to recognize the clinical risk factors and identifying characteristics of the high-risk population to optimize the approach to prevention and treatment. Specifically, this work could benefit local practitioners to better understand the most important factors contributing to mortality due to COVID-19 in this region, for example, how older patients, an altered BMI, a history of HBV-HCV, an impaired mental status and altered platelet levels are markers that should alert healthcare providers to establish early treatment. Additionally, this information can provide us with potential indicators to consider in future outbreaks and highlight and document the need for the establishment of an adequate hospital and community epidemiological surveillance and education system, particularly in rural and northern Peru. Further research should follow up the survivors with the risk factors presented to assess the long-term impact of the disease on their quality of life, e.g., it is possible that this population may have sequelae that considerably affects their physical, mental, interpersonal and environmental health.

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Informed Consent Statement: All the survey participants were well versed on the study intentions and were required to consent before enrollment.

Data Availability Statement: The data presented in this study are available on request from the corresponding author.

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References

1. Sánchez-Duque, J.A.; Arce-Villalobos, L.R.; Rodríguez-Morales, A.J. Coronavirus disease 2019 (COVID-19) in Latin America: Role of primary care in preparedness and response. *Aten. Primaria* **2020**, *52*, 369–372. [[CrossRef](#)]
2. Valdez Huarcaya, W.; Miranda Monzón, J.A.; Napanga Saldaña, E.O.; Driver, C.R. Impact of COVID-19 on mortality in Peru using triangulation of multiple data sources. *Rev. Panam. Salud Pública* **2022**, *46*, e53. [[CrossRef](#)] [[PubMed](#)]
3. Herrera-Añazco, P.; Uyen-Cateriano, A.; Mezones-Holguin, E.; Taype-Rondan, A.; Mayta-Tristan, P.; Malaga, G.; Hernandez, A.V. Some Lessons That Peru Did Not Learn before the Second Wave of COVID-19. *Int. J. Health Plann. Manag.* **2021**, *36*, 995–998. [[CrossRef](#)] [[PubMed](#)]

4. Talic, S.; Shah, S.; Wild, H.; Gasevic, D.; Maharaj, A.; Ademi, Z.; Li, X.; Xu, W.; Mesa-Eguiagaray, I.; Rostron, J.; et al. Effectiveness of Public Health Measures in Reducing the Incidence of COVID-19, SARS-CoV-2 Transmission, and COVID-19 Mortality: Systematic Review and Meta-Analysis. *BMJ* **2021**, *375*, e068302. [[CrossRef](#)] [[PubMed](#)]
5. Antiporta, D.A.; Cutipé, Y.L.; Mendoza, M.; Celentano, D.D.; Stuart, E.A.; Bruni, A. Depressive Symptoms among Peruvian Adult Residents amidst a National Lockdown during the COVID-19 Pandemic. *BMC Psychiatry* **2021**, *21*, 111. [[CrossRef](#)]
6. Zhang, S.X.; Sun, S.; Afshar Jahanshahi, A.; Alvarez-Risco, A.; Ibarra, V.G.; Li, J.; Patty-Tito, R.M. Developing and Testing a Measure of COVID-19 Organizational Support of Healthcare Workers—Results from Peru, Ecuador, and Bolivia. *Psychiatry Res.* **2020**, *291*, 113174. [[CrossRef](#)]
7. Alvarez-Risco, A.; Del-Aguila-Arcatales, S.; Yáñez, J.A.; Rosen, M.A.; Mejia, C.R. Influence of Technostress on Academic Performance of University Medicine Students in Peru during the COVID-19 Pandemic. *Sustainability* **2021**, *13*, 8949. [[CrossRef](#)]
8. Villena-Tejada, M.; Vera-Ferchau, I.; Cardona-Rivero, A.; Zamalloa-Cornejo, R.; Quispe-Florez, M.; Frisancho-Triveño, Z.; Abarca-Meléndez, R.C.; Alvarez-Sucari, S.G.; Mejia, C.R.; Yáñez, J.A. Use of Medicinal Plants for COVID-19 Prevention and Respiratory Symptom Treatment during the Pandemic in Cusco, Peru: A Cross-Sectional Survey. *PLoS ONE* **2021**, *16*, e0257165. [[CrossRef](#)]
9. Roupe, K.A.; Helms, G.L.; Halls, S.C.; Yáñez, J.A.; Davies, N.M. Preparative Enzymatic Synthesis and HPLC Analysis of Rhapontigenin: Applications to Metabolism, Pharmacokinetics and Anti-Cancer Studies. *J. Pharm. Pharm. Sci.* **2005**, *8*, 374–386.
10. Yáñez, J.A.; Remsberg, C.M.; Takemoto, J.K.; Vega-Villa, K.R.; Andrews, P.K.; Sayre, C.L.; Martinez, S.E.; Davies, N.M. Polyphenols and Flavonoids: An Overview. In *Flavonoid Pharmacokinetics*; John Wiley & Sons, Ltd.: Hoboken, NJ, USA, 2012; pp. 1–69, ISBN 978-1-118-46852-4.
11. Munayco, C.; Chowell, G.; Tariq, A.; Undurraga, E.A.; Mizumoto, K. Risk of Death by Age and Gender from CoVID-19 in Peru, March–May, 2020. *Aging* **2020**, *12*, 13869–13881. [[CrossRef](#)]
12. Fried, M.W.; Crawford, J.M.; Mospan, A.R.; Watkins, S.E.; Munoz, B.; Zink, R.C.; Elliott, S.; Burleson, K.; Landis, C.; Reddy, K.R.; et al. Patient Characteristics and Outcomes of 11 721 Patients With Coronavirus Disease 2019 (COVID-19) Hospitalized Across the United States. *Clin. Infect. Dis.* **2021**, *72*, e558–e565. [[CrossRef](#)] [[PubMed](#)]
13. Garg, S.; Kim, L.; Whitaker, M.; O’Halloran, A.; Cummings, C.; Holstein, R.; Prill, M.; Chai, S.J.; Kirley, P.D.; Alden, N.B.; et al. Hospitalization Rates and Characteristics of Patients Hospitalized with Laboratory-Confirmed Coronavirus Disease 2019—COVID-NET, 14 States, March 1–30, 2020. *Morb. Mortal. Wkly. Rep.* **2020**, *69*, 458–464. [[CrossRef](#)] [[PubMed](#)]
14. Mejía, F.; Medina, C.; Cornejo, E.; Morello, E.; Vásquez, S.; Alave, J.; Schwalb, A.; Málaga, G. Oxygen Saturation as a Predictor of Mortality in Hospitalized Adult Patients with COVID-19 in a Public Hospital in Lima, Peru. *PLoS ONE* **2020**, *15*, e0244171. [[CrossRef](#)] [[PubMed](#)]
15. Valenzuela, G.V.; Rodriguez-Morales, A.J.; Mamani, R.; Ayala, R.; Pérez, K.; Sarmiento, C.; Calcino, J.; García, L.; Amado, J. Cardiovascular Risk Factors and Evolution of Patients Attended with COVID-19 in a National Reference Hospital from Lima, Peru. *Rev. Peru. Investig. Salud* **2021**, *5*, 195–200. [[CrossRef](#)]
16. Vizcardo, D.; Salvador, L.F.; Nole-Vara, A.; Dávila, K.P.; Alvarez-Risco, A.; Yáñez, J.A.; Mejia, C.R. Sociodemographic Predictors Associated with the Willingness to Get Vaccinated against COVID-19 in Peru: A Cross-Sectional Survey. *Vaccines* **2021**, *10*, 48. [[CrossRef](#)]
17. Izcovich, A.; Ragusa, M.A.; Tortosa, F.; Lavena Marzio, M.A.; Agnoletti, C.; Bengolea, A.; Ceirano, A.; Espinosa, F.; Saavedra, E.; Sanguine, V.; et al. Prognostic Factors for Severity and Mortality in Patients Infected with COVID-19: A Systematic Review. *PLoS ONE* **2020**, *15*, e0241955. [[CrossRef](#)] [[PubMed](#)]
18. Booth, A.; Reed, A.B.; Ponzio, S.; Yassaee, A.; Aral, M.; Plans, D.; Labrique, A.; Mohan, D. Population Risk Factors for Severe Disease and Mortality in COVID-19: A Global Systematic Review and Meta-Analysis. *PLoS ONE* **2021**, *16*, e0247461. [[CrossRef](#)]
19. Huang, I.; Lim, M.A.; Pranata, R. Diabetes Mellitus Is Associated with Increased Mortality and Severity of Disease in COVID-19 Pneumonia—A Systematic Review, Meta-Analysis, and Meta-Regression. *Diabetes Metab. Syndr. Clin. Res. Rev.* **2020**, *14*, 395–403. [[CrossRef](#)]
20. Dessie, Z.G.; Zewotir, T. Mortality-Related Risk Factors of COVID-19: A Systematic Review and Meta-Analysis of 42 Studies and 423,117 Patients. *BMC Infect. Dis.* **2021**, *21*, 855. [[CrossRef](#)]
21. Alves, V.P.; Casemiro, F.G.; de Araujo, B.G.; de Lima, M.A.S.; de Oliveira, R.S.; de Fernandes, F.T.S.; Gomes, A.V.C.; Gregori, D. Factors Associated with Mortality among Elderly People in the COVID-19 Pandemic (SARS-CoV-2): A Systematic Review and Meta-Analysis. *Int. J. Environ. Res. Public Health* **2021**, *18*, 8008. [[CrossRef](#)]
22. Vardavas, C.I.; Mathioudakis, A.G.; Nikitara, K.; Stamatielopoulos, K.; Georgiopoulos, G.; Phalkey, R.; Leonardi-Bee, J.; Fernandez, E.; Carnicer-Pont, D.; Vestbo, J.; et al. Prognostic Factors for Mortality, Intensive Care Unit and Hospital Admission Due to SARS-CoV-2: A Systematic Review and Meta-Analysis of Cohort Studies in Europe. *Eur. Respir. Rev.* **2022**, *31*, 220098. [[CrossRef](#)] [[PubMed](#)]
23. Bepouka, B.; Mayasi, N.; Mandina, M.; Longokolo, M.; Odio, O.; Mangala, D.; Mbula, M.; Kayembe, J.M.; Situakibanza, H. Risk Factors for Mortality in COVID-19 Patients in Sub-Saharan Africa: A Systematic Review and Meta-Analysis. *PLoS ONE* **2022**, *17*, e0276008. [[CrossRef](#)] [[PubMed](#)]
24. León-Jiménez, F.; Vives-Kufof, C.; Failoc-Rojas, V.E.; Valladares-Garrido, M.J. Mortality in patients hospitalized with COVID-19 in northern Peru. *Rev. Med. Chile* **2021**, *149*, 1459–1466. [[CrossRef](#)] [[PubMed](#)]

25. Zuniga-Moya, J.C.; Norwood, D.A.; Romero Reyes, L.E.; Barrueto Saavedra, E.; Diaz, R.; Fajardo, W.C.; Pineda, A.; Torres, D.; Barahona, R.; Leiva, S.O.; et al. Epidemiology, Outcomes, and Associated Factors of Coronavirus Disease 2019 (COVID-19) Reverse Transcriptase Polymerase Chain Reaction-Confirmed Cases in the San Pedro Sula Metropolitan Area, Honduras. *Clin. Infect. Dis.* **2021**, *72*, e476–e483. [[CrossRef](#)]
26. Resolución Ministerial, N. ° 839-2020-MINSA. Available online: <https://www.gob.pe/institucion/minsa/normas-legales/1264399-839-2020-minsa> (accessed on 11 December 2022).
27. Chilimuri, S.; Sun, H.; Alemam, A.; Mantri, N.; Shehi, E.; Tejada, J.; Yugay, A.; Nayudu, S.K. Predictors of Mortality in Adults Admitted with COVID-19: Retrospective Cohort Study from New York City. *West. J. Emerg. Med.* **2020**, *21*, 779–784. [[CrossRef](#)]
28. Li, M.; Cheng, B.; Zeng, W.; Chen, S.; Tu, M.; Wu, M.; Tong, W.; Wang, S.; Huang, Y.; Long, W.; et al. Analysis of the Risk Factors for Mortality in Adult COVID-19 Patients in Wuhan: A Multicenter Study. *Front. Med.* **2020**, *7*, 545. [[CrossRef](#)]
29. Fumagalli, C.; Rozzini, R.; Vannini, M.; Coccia, F.; Cesaroni, G.; Mazzeo, F.; Cola, M.; Bartoloni, A.; Fontanari, P.; Lavorini, F.; et al. Clinical Risk Score to Predict In-Hospital Mortality in COVID-19 Patients: A Retrospective Cohort Study. *BMJ Open* **2020**, *10*, e040729. [[CrossRef](#)]
30. Heberto, A.B.; Carlos, P.C.J.; Antonio, C.R.J.; Patricia, P.P.; Enrique, T.R.; Danira, M.P.J.; Benito, G.Á.E.; Alfredo, M.R.J. Implications of Myocardial Injury in Mexican Hospitalized Patients with Coronavirus Disease 2019 (COVID-19). *Int. J. Cardiol. Heart Vasc.* **2020**, *30*, 100638. [[CrossRef](#)]
31. Skorin, I.; Carrillo, R.; Perez, C.P.; Sanchez, N.; Parra, J.; Troncoso, P.; Uribe-San-Martin, R. EEG Findings and Clinical Prognostic Factors Associated with Mortality in a Prospective Cohort of Inpatients with COVID-19. *Seizure* **2020**, *83*, 1–4. [[CrossRef](#)]
32. Acosta, G.; Escobar, G.; Bernaola, G.; Alfaro, J.; Taype, W.; Marcos, C.; Amado, J. Description of patients with severe COVID-19 treated in a national referral hospital in Peru. *Rev. Peru. Med. Exp. Salud Publica* **2020**, *37*, 253–258. [[CrossRef](#)]
33. Boletines Epidemiológicos. Available online: <https://www.dge.gob.pe/portalnuevo/publicaciones/boletines-epidemiologicos/> (accessed on 11 December 2022).
34. Vargas, C.M. Reflexiones sobre el COVID-19, el Colegio Médico del Perú y la Salud Pública. *Acta Med. Peru.* **2020**, *37*, 8–10. [[CrossRef](#)]
35. Garcia, P.J.; Alarcón, A.; Bayer, A.; Buss, P.; Guerra, G.; Ribeiro, H.; Rojas, K.; Saenz, R.; Salgado de Snyder, N.; Solimano, G.; et al. COVID-19 Response in Latin America. *Am. J. Trop. Med. Hyg.* **2020**, *103*, 1765–1772. [[CrossRef](#)] [[PubMed](#)]
36. Neyra-León, J.; Huancahuari-Nuñez, J.; Díaz-Monge, J.C.; Pinto, J.A. The Impact of COVID-19 in the Healthcare Workforce in Peru. *J. Public Health Policy* **2021**, *42*, 182–184. [[CrossRef](#)] [[PubMed](#)]
37. Kang, S.J.; Jung, S.I. Age-Related Morbidity and Mortality among Patients with COVID-19. *Infect. Chemother.* **2020**, *52*, 154–164. [[CrossRef](#)]
38. Leung, C. Risk Factors for Predicting Mortality in Elderly Patients with COVID-19: A Review of Clinical Data in China. *Mech. Ageing Dev.* **2020**, *188*, 111255. [[CrossRef](#)]
39. Zhang, J.-J.; Dong, X.; Cao, Y.-Y.; Yuan, Y.-D.; Yang, Y.-B.; Yan, Y.-Q.; Akdis, C.A.; Gao, Y.-D. Clinical Characteristics of 140 Patients Infected with SARS-CoV-2 in Wuhan, China. *Allergy* **2020**, *75*, 1730–1741. [[CrossRef](#)]
40. Zhou, F.; Yu, T.; Du, R.; Fan, G.; Liu, Y.; Liu, Z.; Xiang, J.; Wang, Y.; Song, B.; Gu, X.; et al. Clinical Course and Risk Factors for Mortality of Adult Inpatients with COVID-19 in Wuhan, China: A Retrospective Cohort Study. *Lancet* **2020**, *395*, 1054–1062. [[CrossRef](#)]
41. Blagosklonny, M.V. From Causes of Aging to Death from COVID-19. *Aging* **2020**, *12*, 10004–10021. [[CrossRef](#)]
42. Quah, P.; Li, A.; Phua, J. Mortality Rates of Patients with COVID-19 in the Intensive Care Unit: A Systematic Review of the Emerging Literature. *Crit. Care* **2020**, *24*, 285. [[CrossRef](#)]
43. Sunjaya, A.P.; Allida, S.M.; Di Tanna, G.L.; Jenkins, C. Asthma and Risk of Infection, Hospitalization, ICU Admission and Mortality from COVID-19: Systematic Review and Meta-Analysis. *J. Asthma* **2022**, *59*, 866–879. [[CrossRef](#)]
44. Qian, Z.; Alaa, A.M.; van der Schaar, M.; Ercole, A. Between-Centre Differences for COVID-19 ICU Mortality from Early Data in England. *Intensive Care Med.* **2020**, *46*, 1779–1780. [[CrossRef](#)] [[PubMed](#)]
45. Zhao, Z.; Chen, A.; Hou, W.; Graham, J.M.; Li, H.; Richman, P.S.; Thode, H.C.; Singer, A.J.; Duong, T.Q. Prediction Model and Risk Scores of ICU Admission and Mortality in COVID-19. *PLoS ONE* **2020**, *15*, e0236618. [[CrossRef](#)] [[PubMed](#)]
46. Auld, S.C.; Caridi-Scheible, M.; Blum, J.M.; Robichaux, C.; Kraft, C.; Jacob, J.T.; Jabaley, C.S.; Carpenter, D.; Kaplow, R.; Hernandez-Romieu, A.C.; et al. ICU and Ventilator Mortality Among Critically Ill Adults With Coronavirus Disease 2019. *Crit. Care Med.* **2020**, *48*, e799–e804. [[CrossRef](#)] [[PubMed](#)]
47. Mannucci, E.; Silverii, G.A.; Monami, M. Saturation of Critical Care Capacity and Mortality in Patients with the Novel Coronavirus (COVID-19) in Italy. *Trends Anaesth. Crit. Care* **2020**, *33*, 33–34. [[CrossRef](#)]
48. Hu, B.; Huang, S.; Yin, L. The Cytokine Storm and COVID-19. *J. Med. Virol.* **2021**, *93*, 250–256. [[CrossRef](#)]
49. Ragab, D.; Salah Eldin, H.; Taeimah, M.; Khattab, R.; Salem, R. The COVID-19 Cytokine Storm; What We Know So Far. *Front. Immunol.* **2020**, *11*, 1446. [[CrossRef](#)]
50. Vaninov, N. In the Eye of the COVID-19 Cytokine Storm. *Nat. Rev. Immunol.* **2020**, *20*, 277. [[CrossRef](#)]
51. Zhu, Y.; Zhang, J.; Li, Y.; Liu, F.; Zhou, Q.; Peng, Z. Association between Thrombocytopenia and 180-Day Prognosis of COVID-19 Patients in Intensive Care Units: A Two-Center Observational Study. *PLoS ONE* **2021**, *16*, e0248671. [[CrossRef](#)]

52. Lee, J.Y.; Kim, H.A.; Huh, K.; Hyun, M.; Rhee, J.-Y.; Jang, S.; Kim, J.-Y.; Peck, K.R.; Chang, H.-H. Risk Factors for Mortality and Respiratory Support in Elderly Patients Hospitalized with COVID-19 in Korea. *J. Korean Med. Sci.* **2020**, *35*, e223. [[CrossRef](#)]
53. Yong, S.J. Persistent Brainstem Dysfunction in Long-COVID: A Hypothesis. *ACS Chem. Neurosci.* **2021**, *12*, 573–580. [[CrossRef](#)]

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