

Original article

Mortality and associated risk factors in patients with COVID-19 A hospital-based study in Ecuador









*Mortalidad y factores de riesgo asociados en pacientes con COVID-19
Un estudio hospitalario en Ecuador*

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-  Edy Quizhpe ^{a,b,c}, edy.quizhpe@umu.se
 -  Eduardo Montalvo ^b, eduardo.montalvo@hgdc.gob.ec
 -  Maritza Paéz ^b, maritza.paez@hgdc.gob.ec
 -  Tatiana Guevara ^b, tatiana.guevara@hgdc.gob.ec
 -  Danny Flores ^b, danny.flores@hgdc.gob.ec
 -  Dennise Costales ^b, denissempe@hotmail.com
 -  Luis Vidal ^b, luis.vidal@hgdc.gob.ec
 -  Augusto Maldonado ^{b, d}, mald1544@hotmail.com
- a. Umea University. Umea, Sweden.
b. General Teaching Calderon Hospital. Quito, Ecuador.
c. San Francisco of Quito University. Quito, Ecuador.
d. Hofstra/Northwell University. New York, United States.

Correspondence: Edy Quizhpe **E-mail:** edy.quizhpe@umu.se

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Abstract

Background: Since the coronavirus disease 2019 (COVID-19) pandemic, increased mortality has been reported in Ecuador, with an additional 59,000 deaths during 2019–2020, approximately doubling the mortality from other causes. Although Latin America has faced epidemics of non-communicable diseases over the past decades, the devastating effect of COVID-19 is unprecedented. This study aimed to describe the clinical characteristics and risk factors observed in patients with COVID-19 treated in a general hospital in Ecuador. **Methods:** This hospital-based study was conducted from March to July 2020. We obtained data from the clinical records of 157 adult men and women diagnosed with COVID-19 using the reverse transcription-polymerase chain reaction test and admitted to an emergency service room. We used descriptive statistics and performed a chi-square test and logistic regression analysis to analyze the associations between the categorical variables. **Results:** We found that the overall mortality rate was 37 % and was higher in men (39 %) than in women (31 %). We observed a high prevalence of comorbidities (45 %) related to non-communicable diseases, particularly diabetes and hypertension, significantly associated with mortality rates. Similarly, distribution by gender and abnormalities in blood markers such as leukocytes, PO2, and D-dimer increased the risk of death. **Conclusions:** The high and extensive prevalence of non-communicable diseases was a risk factor for high mortality among patients diagnosed with COVID-19. In Latin American countries, healthcare systems continue to experience severe challenges in treating patients with such comorbid health conditions.

Keywords: COVID-19. Mortality. Ecuador. Non-communicable Diseases. Latin America.

Resumen

Antecedentes: Desde la pandemia de la enfermedad por coronavirus 2019 (COVID-19), se ha informado un aumento de la mortalidad en Ecuador, con 59 000 muertes adicionales durante 2019-2020, aproximadamente el doble de la mortalidad por otras causas. Aunque América Latina ha enfrentado epidemias de enfermedades no transmisibles en las últimas décadas, el efecto devastador de la COVID-19 no tiene precedentes. Este estudio tuvo como objetivo describir las características clínicas y los factores de riesgo observados en pacientes con COVID-19 atendidos en un hospital general de Ecuador. **Métodos:** Este estudio hospitalario se realizó de marzo a julio de 2020. Se obtuvo datos de las historias clínicas de 157 hombres y mujeres adultos diagnosticados con COVID-19 mediante la prueba de reacción en cadena de la polimerasa con transcriptasa inversa e ingresados en una sala de servicio de emergencia. Se utilizó estadística descriptiva y se realizó una prueba de chi-cuadrado y análisis de regresión logística para analizar las asociaciones entre las variables categóricas. **Resultados:** Encontramos que la tasa de mortalidad global fue del 37 % y fue mayor en hombres (39 %) que en mujeres (31 %). Se observó una alta prevalencia de comorbilidades (45 %) relacionadas con enfermedades no transmisibles, en particular diabetes e hipertensión, asociadas significativamente con las tasas de mortalidad. De manera similar, la distribución por género y las anomalías en los marcadores sanguíneos como leucocitos, PO₂ y dímero D aumentaron el riesgo de muerte. **Conclusiones:** La alta prevalencia de enfermedades no transmisibles fue un factor de riesgo de alta mortalidad entre los pacientes diagnosticados con COVID-19. En los países latinoamericanos, los sistemas de salud continúan experimentando desafíos severos en el tratamiento de pacientes con tales condiciones de salud comórbidas.

30 Palabras clave: COVID-19. Mortalidad. Ecuador. Enfermedades no Transmisibles. América Latina.

Introduction

The global spread of the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that causes coronavirus disease 2019 (COVID-19) has severely damaged economies and health systems worldwide. In Latin America, COVID-19 has mainly affected countries with high socioeconomic inequalities, such as Brazil, Peru, and Ecuador, and most of these cases

have been correlated with social determinants such as poverty, humanitarian crises, fragile health systems, and persistent inequalities. Moreover, the continued increase in non-communicable diseases such as obesity and diabetes are likely the main contributors to the elevated mortality rates ¹

Ecuador is a middle-income Latin American country characterized by high socioeconomic inequalities and ethnic diversity ²

Its healthcare system is exceedingly fragmented, with several sub-systems distributed throughout the public and private sectors. The former includes the Ministry of Health and the Ecuadorian Institute of Social Security (Instituto Ecuatoriano de Seguridad Social in Spanish), providing health insurance coverage to the underprivileged and formal sector employees ³

However, the COVID-19 pandemic has resulted in high mortality in Ecuador, ⁴ causing an additional 59000 deaths between 2019 and 2020, and ⁵ approximately doubling the existing mortality from other causes. Very few studies have focused on describing the main clinical characteristics and degree of association between risk factors and mortality at the local level ⁶

The pandemic peaked between 2019 and 2020, creating severe limitations for patients to access healthcare services, particularly intensive care units. ^{7,8}

This study aimed to describe the main clinical characteristics and risk factors associated with mortality in adult patients without health insurance who were admitted into an emergency service room in a hospital in Quito, the capital of Ecuador.

Methods

This hospital-based study recruited 157 patients, both men and women, aged 18 years and above. All patients admitted into the emergency service room for suspected COVID-19 infection in a general hospital in Quito between March to July 2020 were included in the sample. Diagnoses were confirmed by the reverse transcription-polymerase chain reaction (RT-PCR) test.

The main sociodemographic characteristics and clinical data were obtained from the epidemiological surveillance system and the individuals' medical records. The laboratory confirmation of the

SARS-CoV-2 infection was performed using the RT-PCR assay in nasopharyngeal swabs. The time of illness was defined as the date of onset of symptoms such as cough and fever. Furthermore, illness severity was evaluated using the National Early Warning Score 2 (NEWS2) ⁹

The laboratory parameters were evaluated according to those recommended for the city of Quito. Descriptive statistics were calculated for the demographic and clinical data. The chi-square test and logistic regression analysis were employed to evaluate the associations between the variables. The statistical analysis was performed using STATA version 15.0. The Ecuadorian Ethical National Committee approved the protocol of this study of COVID-19 created by the Ecuadorian Ministry of Health.

Results

Demographic and clinical characteristics

Table 1 presents the patients' main characteristics. The proportions of women and men were 48% and 52%, respectively. About 78 % of the patients were aged over 50. Most patients had low educational attainment (61 % had completed only primary school). The average time from the onset of symptoms was 7.4 days, longer in men (8.03) than in women (6.73). Cough (77.07 %) and dyspnea (75.64 %) were the most prevalent symptoms, followed by fever (58.60 %) and fatigue (55.41 %), all of which were more common in men.

Additionally, the association between symptoms and mortality showed no significant differences. Overall, while anosmia, runny nose, exanthema, and conjunctive injection were almost absent, only fever showed statistically significant differences between the sexes ($P=0.00$). All patients had tachypnea (a mean respiratory frequency of 27.17) and oxygen saturation below 90% (76.96 %; women 76.85 %; men 77.06 %). Those patients who died had significantly lower levels of saturation (69.27 %; $P=0.00$).

Mortality distribution

The mortality and symptom severity distribution among patients are presented in Table 2.

The mean score of the NEWS2 was 6.68 points, indicating a high proportion of severe cases; all the values were higher for men than for women.

Furthermore, 35.03 % of the patients died (39.02 % men and 30.67 % women). However, significant mortality ($P=0.02$) was observed in the patients with Medium NEWS2 scores as compared to those with High NEWS2 scores (54.55 % and 42.82 %, respectively), which were found to be higher in men in cases with High NEWS2 score (71.88%).

Additionally, increased mortality (52.73 %) was observed in patients aged 65 years and above and was higher in women (56.52 %). Nevertheless, in the 50–64 years group, men had significantly higher mortality ($P=0.02$), more than twice that of women (43.75 % and 17.39 %, respectively).

The multi-regression analysis was adjusted for age. The probability of death increased with each day of illness (OR: 1.04, 95% IC: 0.95-1.12) and was higher in women (OR: 1.96, 95 % IC: 0.82-3.22). The presence of comorbidities increased this probability significantly (OR: 2.38, 95% IC: 1.14-4.93). Patients with diabetes (OR: 2.23, 95% IC: 0.76-6.48) and those with hypertension (OR: 1.25, 95 % IC: 0.51-3.08) were two times more likely to succumb to it.

Although diabetes and hypertension increased the risk of death, it was not significant (OR: 2.43, 95 % IC: 0.82-7.21). The analysis of sex differences, based on laboratory findings, revealed poor health outcomes for men regarding the severity of their symptoms and mortality, whereas women suffered mostly from comorbidities and were at an increased risk of death based on their age.

Table 1. Demographic and clinical characteristics of patients with COVID-19 admitted to the hospital

Variables	Total N (%)	Patients died	Patients survived	P
	157 (100)	55 (35.03)	102 (64.97)	
Age group (years)				
20 to 49	35 (22.29)	8 (14.55)	27 (26.47)	0.03
50 to 64	60 (38.22)	18 (32.73)	42 (41.18)	
Above 65	62 (39.49)	29 (52.73)	33 (32.35)	
Education				
None	23 (14.65)	11 (20.00)	12 (11.76)	0.27
Primary	96 (61.15)	29 (52.73)	67 (65.69)	
Secondary	33 (21.02)	14 (25.45)	19 (18.63)	
High	5 (3.18)	1 (1.82)	4 (3.92)	
Comorbidities				
Yes	71 (45.22)	20 (36.36)	51 (50.00)	0.10
No	86 (54.78)	35 (63.64)	51 (50.00)	
Chronic diseases				
Hypertension	28 (17.83)	10 (18.18)	18 (17.65)	0.93
Diabetes	23 (14.65)	5 (9.09)	18 (17.65)	0.14
Signs and Symptoms				
Time of illness (days)	7.4 (6.73-8.06)	6.94 (8.85-8.03)	7.6 (6.85-8.48)	0.29
Cough	121 (77.07)	40 (72.73)	81 (79.41)	0.34
Dyspnea	118 (75.64)	45 (81.82)	73 (72.28)	0.18
Fever	92 (58.60)	24 (43.64)	68 (66.67)	0.00
Fatigue	87 (55.41)	28 (50.91)	59 (57.84)	0.40
Sore throat	27 (17.20)	10 (18.18)	17 (16.67)	0.81
Cephalaea	26 (16.56)	10 (18.18)	16 (15.69)	0.68
Productive cough	26 (16.56)	8 (14.55)	18 (17.65)	0.61
Diarrhea	23 (14.65)	6 (10.91)	17 (16.67)	0.33
Myalgia	17 (10.83)	9 (16.36)	8 (7.84)	0.10
Nausea	9 (5.73)	5 (9.09)	4 (3.92)	0.18
Runny nose	7 (4.46)	2 (3.64)	5 (4.90)	0.71
Anosmia	2 (1.27)	0 (0.00)	2 (1.96)	0.29
Basic measures				
Temperature	37.18 (37.04-37.32)	37.16 (36.92-37.40)	37.19 (37.01-37.37)	0.82
Respiratory frequency	27 (25.97-28.37)	29 (26.49-30.88)	26 (24.94-27.78)	0.06
Oxygen saturation (%)	77 (74.69-79.22)	69 (64.84-73.69)	81 (78.89-83.31)	0.00
Systolic blood pressure	127 (123.11-129.90)	124 (117.96-130.25)	128 (123.70-131.90)	0.30
Pulse (bpm)	99 (96.03-102.09)	100 (95.33-106.19)	100 (96.26-105.22)	0.41
Glasgow scale	15 (14.72-14.99)	15 (14.21 - 14.98)	15 (15.00 - 15.00)	0.00

Table 2. Distribution of patients with COVID-19 hospitalized according to symptom severity and mortality by sex and age

Severity of illness	Total N (%)	Women N (%)	Men N (%)	P
NEWS2 Score	6.68 (6.36-6.99)	6.44 (5.97-6.90)	6.90 (6.48-7.32)	0.14
NEWS2 Score 1 -4 (LOW)	22 (14.01)	13 (17.33)	9 (10.98)	
NEWS2 Score 5 -6 (MEDIUM)	47 (29.94)	25 (33.33)	22 (26.83)	0.24
NEWS2 Score >7 (HIGH)	88 (56.05)	37 (49.33)	51 (62.20)	
Mortality				
Overall	55 (35.03)	23 (30.67)	32 (39.02)	0.27
Mortality by NEWS2 Score				
NEWS2 Score 1 -4 (LOW)	2 (3.64)	0 (0.00)	2 (6.25)	
NEWS2 Score 5 -6 (MEDIUM)	30 (54.55)	8 (34.78)	7 (21.88)	0.01
NEWS2 Score >7 (HIGH)	23 (41.82)	15 (65.22)	23 (71.88)	
Mortality by age group				
20 to 49	8 (14.55)	6 (26.09)	2 (6.25)	
50 to 64	18 (32.73)	4 (17.39)	14 (43.75)	0.03
Above 65	29 (52.73)	13 (56.52)	16 (50.00)	

Laboratory findings

Table 3 presents the laboratory findings according to sex differences and final health outcomes.

The mean number of leukocytes and neutrophils was higher than estimated. Furthermore, the lymphocyte count indicated lymphopenia in men but not in women ($P= 0.02$). The patients who died had significantly greater leukocytes and neutrophils than those who survived ($P= 0.00$).

Those who died, specifically men, had significantly elevated inflammatory and infectious markers ($P= 0.05$). Most of the patients presented hypoxia (PO_2 mean: 56.58 mmHg (53.45-59.72)); however, this difference was insignificant between men and women.

Table 3. Laboratory findings in patients with COVID-19 hospitalized by final health outcome

White cells	Total (mean)	Patients died	Patients survive	P
Leukocytes ($<4.5 \times 10^9/L$ - $>10 \times 10^9/L$) N=156	10.21 (9.45-10.97)	13.03 (11.62-14.45)	8.69 (7.94-9.44)	0.00
Lymphocytes ($<1.1 \times 10^9/L$ - $>3.2 \times 10^9/L$) N=156	1.15 (1.06-1.24)	1.13 (0.93-1.33)	1.16 (1.08-1.25)	0.72
Neutrophils ($<2.2 \times 10^9/L$ - $>4.8 \times 10^9/L$) N=156	8.52 (7.78 - 9.26)	11.19 (9.82-12.56)	7.08 (6.34-7.82)	0.00
Platelets ($<150 \times 10^9/L$ - $>450 \times 10^9/L$) N=156	280.23 (265.99-294.48)	281.23 (261.06-301.40)	279.69 (260.41-298.97)	0.91
Blood chemistry				
Fibrinogen (<350 mg/dl) N=96	639.82 (606.40-673.23)	634.52 (571.38-697.65)	643.29 (604.87-681.71)	0.80
Creatinine (<1.25 mg/dl) N=152	1.23 (0.96-1.49)	1.36 (1.05-1.66)	1.16 (0.79-1.53)	0.48
Urea (<42.9 mg/dl) N=154	46.77 (40.84-52.70)	59.46 (46.93-71.99)	39.99 (34.07-45.91)	0.00
TP (<13.7 s) N=140	12.12 (11.85-12.40)	12.44 (12.12-12.76)	11.95 (11.56-12.34)	0.09
TTP (<36.2 s) N=140	34.41 (33.34-35.48)	35.15 (33.21-37.10)	34.00 (32.72-35.28)	0.30
AST (<34 U/L) N= 145	53.84 (48.15-59.53)	63.13 (50.01-76.26)	48.79 (43.71-53.88)	0.01
ALT (<55 U/L) N=140	51.65 (43.43-59.86)	59.57 (37.62-81.52)	47.64 (41.79-53.49)	0.17
LDH (M: <275 U/L W: <290 U/L) N=124	443.38 (412.08 - 474.6)	534.91 (472.89-596.92)	396.49 (365.08-427.91)	0.00
PCR (0.5 mg/dl) N=101	17.12 (13.31-20.94)	23.34 (12.31-34.37)	13.97 (12.53-15.42)	0.02
D-dimer (<500 ug/ml) N=113	1685.35 (1228.13-2142.57)	2998.11 (1671.68-4324.55)	1120.36 (850.52-1390.20)	0.00
Troponin (39.2 pg/ml) N=85	53.54 (21.40-85.59)	64.06 (29.09-99.04)	48.01 (2.24-93.95)	0.63
Ferritin (<274 ng/ml) N=127	964.6 (837.9 - 1091.2)	957.37 (765.95 - 1148.79)	967.72 (804.29 - 1131.15)	0.94
PCO ₂ (40 mmHg) N=149	32.51 (31.20-33.81)	33.73 (30.61-36.84)	31.82 (30.72-32.92)	0.16
PO ₂ (60 mmHg) N =149	56.58 (53.45-59.72)	52.98 (47.72-58.25)	58.61 (54.69-62.52)	0.08
Lactate (2.0 mmol/L) N=149	2.19 (1.96-2.41)	2.72 (2.18-3.25)	1.89 (1.72-2.06)	0.00

Discussion

Comorbidities were identified as the leading risk factor for higher mortality in COVID-19 cases during the study. Symptoms such as cough, dyspnea, fever, and fatigue indicated that they had severe acute respiratory syndrome. These findings are consistent with the World Health Organization's concern that people with these specific clinical characteristics are at greater risk of contracting COVID-19¹⁰⁻¹². Furthermore, these results conform to the initial cases reported in China¹³⁻¹⁵.

Our research highlights the risk factors associated with high mortality, as previous studies conducted in Peru and Brazil¹⁶.

The high prevalence of comorbidities such as hypertension (44.6 %) and diabetes (33.5 %) in Ecuador and other Latin American countries may be key factors contributing to the rise in their mortality rate compared with the other countries¹⁷⁻¹⁹.

Similar to previous research, we found that patients with fluctuations in blood inflammatory reaction markers had the weakest prognosis of health outcomes²⁰.

Specifically, men had significantly clinical severe and laboratory findings, which can be explained by their immune system's response to genetic issues²¹.

The increased probability of death in women could be due to comorbidities such as obesity, diabetes, and hypothyroidism, as reported by several studies^{22,23}.

Moreover, our results highlighted the association statistically significant between biomarkers such as D dimer, LDH, PO₂, and urea as a predictor of mortality²⁴.

Nevertheless, this research has certain limitations. The evaluated patients were recruited from a single hospital; therefore, the results may not be nationally representative of the situation. In addition, many patients were unable to access the RT-PCR test due to several factors, such as illness severity, limited availability of testing kits, and lack of time for sampling, which could have resulted in an under-registration of the mortality cases during this period.

Conclusion

This study increases the understanding of the clinical course of infection and its correlation with several risk factors. Mortality was strongly related to the presence of diabetes and hypertension in Ecuador. The presence of these comorbidities and lack of access to health care services may have increased the mortality in patients with COVID-19. We recommend addressing groups with these specific clinical characteristics on a priority basis due to the high prevalence in the regional context. Additionally, specific medical scales and blood markers during health care must be considered in medical practice.

Abbreviations:

AST: Aspartate aminotransferase, PO₂: partial pressure of oxygen, COVID-19: coronavirus disease 2019.

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