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BRIEF COMMUNICATION

Unexpected high frequency of early mortality in COVID-19: a single-centre experience during the first wave of the pandemic

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Abstract

We report the high frequency of early mortality in COVID-19 patients (48.6% of 72 deaths). Early deaths were not explained by differences in age, sex and comorbidities, but they had a more severe disease at hospital admission compared with late deaths. These data highlight the importance of outpatient monitoring for the early identification of COVID-19 patients who require hospital admission.

As the outbreak of severe acute respiratory syndrome, coronavirus 2 (SARS-CoV-2) infection has spread globally, more information is emerging regarding the frequency and causes of mortality and the factors related with it. The risk of mortality is higher in older populations and in patients with comorbid conditions such as chronic cardiovascular disease, diabetes mellitus and chronic pulmonary disease.[1] However, fatality rates vary according to location, from 0.7% in South Korea to 6.2% in Italy, and change over time,[2] probably due to the use of different criteria for testing and to differences in the health systems and health status of the population. The frequency of in-hospital deaths also varies between studies.[3] Recently, the Pan American Health Organization reported that the delay in the consultation may be influencing the high mortality rates from coronavirus disease 2019 (COVID-19).[4] Therefore, more data are needed to understand the differences in infection rates and severity among individuals and countries, and their possible impact in guiding decision-making.

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The aim of the present study was to determine frequency, causes and factors associated with early mortality in COVID-19 patients.

This retrospective study was performed in a university hospital in Soledad – Colombia, a city with 800 000 inhabitants. Only deaths of patients with laboratory-confirmed COVID-19 attended in the hospital during the first wave of the pandemic, from March to July 2020, were evaluated. Cases were divided into two groups: (i) patients who arrived at the emergency department with respiratory failure and cardiac arrest and those who died ≤24 h after admission (both classified as the early death group); and (ii) patients who died >24 h after admission (the late death group). The study was approved by the Institutional Ethics Committee (ID204-2020).

During hospitalisation, each patient underwent a complete clinical history and physical examination. Chemistry tests, arterial blood gas determinations and a chest tomography or radiography were also performed. All data were recorded in a computer-assisted protocol. Laboratory-confirmed COVID-19 was defined as a positive polymerase chain reaction test for SARS-CoV-2 in nasopharyngeal samples. Overall mortality was defined as death due to any cause at hospital admission or during hospitalisation. The severity of illness at presentation was quantified using the COVID-GRAM critical illness risk score.[5]

In order to assess factors associated with mortality, early deaths were compared with the rest of the patients. The Chi-squared test for categorical variables and the paired *t*-test for continuous variables were used to detect significant differences between groups. In all the analyses, $P < 0.05$ was considered to be statistically significant. All reported *P*-values are two tailed.

During the study period, 195 patients with laboratory-confirmed COVID-19 required hospital admission. The overall mortality was 36.9% (72 of 195 cases). Early mortality was documented in 35 (48.6%) of 72 deaths (19 arrived at the emergency department with respiratory failure and cardiac arrest and 16 died within ≤24 h after hospital admission). Socio-demographic and clinical features of the study patients are shown in Table 1. Laboratory findings of patients who arrived at the emergency department with respiratory failure and cardiac arrest were not available. Forty-two (58.3%) deaths were older patients (≥65 years). The most common comorbidities were systemic arterial hypertension and diabetes mellitus. Regarding illness severity, almost 90% presented with a high-risk COVID-GRAM score.

No significant differences were documented in age, sex and comorbidities between early and late death cases. Likewise, time from symptoms onset to emergency department admission was similar between study groups. However, lower levels of PaO_2/FiO_2 ratio and moderate/severe acute respiratory distress syndrome criteria ($PaO_2/FiO_2 \leq 200$ mmHg) were more frequent in early deaths compared with late deaths (87.5% vs 54.3%, $P = 0.02$). Early deaths also tended to have higher COVID-GRAM critical illness risk scores at hospital admission. Serum levels of ferritin, C-reactive protein and lactate dehydrogenase were similar between study groups.

Among 53 patients who died during hospital admission, acute respiratory failure secondary to SARS-CoV-2 infection was the most frequent cause of mortality (47 cases), followed by acute myocardial infarction (two cases), and stroke, septic shock related with *Klebsiella pneumoniae* infection, acute heart failure and acute kidney failure (one case each).

Discussion

In this study, early deaths (comprising patients arriving at the emergency department with respiratory and

Table 1 Socio-demographic and clinical features of early and late deaths in patients with COVID-19

	All deaths	Early deaths group	Late deaths group	*P*-value
	n = 72	*n* = 35	*n* = 37	
Age, median (IQR) (years)	67.5 (54.5–78)	66 (54–78.5)	68 (56–77)	0.77
Male sex	50 (69.4)	22 (62.9)	28 (75.7)	0.23
Comorbidities	42 (60.9)	19 (59.4)	23 (62.2)	0.81
Arterial hypertension	29 (42)	13 (40.6)	16 (43.2)	0.82
Chronic cardiac disease	4 (5.8)	1 (3.1)	3 (8.1)	0.61
Chronic pulmonary disease	6 (8.7)	2 (6.2)	4 (10.8)	0.50
Diabetes mellitus	20 (29)	10 (31.2)	10 (27)	0.70
Clinical features				
Time from symptoms onset to ED admission	4 (3–7)	4 (2.5–7)	5 (3–7)	0.41
Fever	43 (59.7)	21 (60)	22 (59.5)	0.96
Cough	44 (61.1)	21 (60)	23 (62.2)	0.85
Dyspnoea	63 (87.5)	29 (82.9)	34 (91.9)	0.33
Laboratory findings†				
PaO_2/FiO_2	151 (64–223.5)	82 (46.5–167.5)	165 (75–258.5)	0.04
Lymphocytes, median (IQR) (cells/uL)	690 (500–990)	690 (500–1430)	710 (490–960)	0.64
Ferritin, median (IQR) (ng/mL)	956 (520–1620.5)	874 (428–1174)	1144 (672.5–1620)	0.38
C-reactive protein, median (IQR) (mg/L)	163 (138.5–174)	170 (154–177.5)	161 (130–173)	0.25
LDH, median (IQR) (U/L)	580 (463–720)	633 (500–809)	560 (457.5–711)	0.52
ALT, median (IQR) (U/L)	45 (28–64)	36 (23–64)	46 (28–64)	0.39
AST, median (IQR) (U/L)	66 (40.92)	72 (43–97)	56 (42–83)	0.79
Treatment				
Antiviral therapy	8 (15.1)	1 (6.2)	7 (18.9)	0.41
Antimicrobial therapy	47 (88.7)	11 (68.8)	36 (97.3)	0.003
Severity score†				
COVID-GRAM critical illness risk score	167.5 (150–204)	196 (167–210)	164 (147–195)	0.06

Data are reported as *n* (%) unless otherwise state.†Laboratory findings and severity score of out-of-hospital deaths were not available. ALT, alanine aminotransferase; AST, aspartate aminotransferase; ED, emergency department; IQR, interquartile range; LDH, lactate dehydrogenase.

cardiac arrest and deaths ≤24 h after admission) were highly frequent, accounting for half of all cases of mortality. Patients who died early formed a specific group with more severe COVID-19 at admission, demonstrated by their lower levels of oxygenation and higher critical illness risk score. Early deaths were not explained by differences in age, sex or comorbidities compared with late deaths.

These results raise the question of why these COVID-19 patients developed respiratory failure and cardiac arrest at home or emergency department or arrived with more severe disease on admission. In this regard, nearly 90% of patients with early mortality had moderate/severe acute respiratory distress syndrome criteria ($PaO_2/FiO_2 \leq 200$ mmHg) at hospital admission. Delay in seeking early medical care may be a factor favouring the unacceptably high frequency of both moderate/severe respiratory failure when arriving at the emergency department and mortality during the first 24 h of hospital admission in these patients. Possible explanations for this delay could be the fear of being infected in the hospital, or misinformation and rumours regarding the disease. During this period, the wide circulation of inaccurate information on social media may have prevented an effective public health response and generated misperception and mistrust;[6] the city residents may have chosen to stay at home, self-medicating with empirical treatment not supported by scientific evidence and seeking health care aid only when their disease was already advanced. Moreover, support for both primary care and outpatient monitoring could favour the early search for medical attention in COVID-19 patients. Outpatient monitoring is paramount to prevent unnecessary medical visits and to identify patients at risk for respiratory decompensation that required outpatient clinic or emergency department evaluation. Outpatients management strategies should take into account the individual clinical and social conditions as well as the accessible resources.[7,8] The delay in early care and the greater severity at hospital admission can limit the usefulness of treatments and procedures that could improve the prognosis of patients with COVID-19.

Other studies have reported a high percentage of out-of-hospital cardiac arrests in patients with suspected or diagnosed COVID-19.[9] According to out-of-hospital cardiac arrest data collected in Italy, there was a significant increase in these events in 2020 during the pandemic. Various pathophysiological processes may account for this relationship; the most probable cause is the occurrence of cardiac arrest secondary to respiratory failure caused by SARS-CoV-2, since this is the most severe complication. However, sudden arrhythmic cardiac death due to direct myocardial damage or pulmonary embolism cannot be ruled out, as these events have been described in other studies.[10,11] Finally, the increased incidence of deaths in SARS-CoV-2 pandemic has also been attributed to the lack of availability of intensive care for patients at a time of limited resources and health system collapse.[3]

This is a single-centre study, and so the frequency and causes of early deaths may vary in other geographical areas with different health systems and socioeconomic characteristics. However, our study highlights that different factors are critical when evaluating COVID-19 mortality, and can explain why severity varies so widely among individuals and countries. More extensive studies from other cities and countries assessing early deaths are now needed. The present study has some other limitations. We included only laboratory-confirmed COVID-19 death cases excluding suspected death cases. In addition, information was lacking on home care, previous medical history, and causes of deaths from some patients, especially in patients arriving at the emergency department with respiratory and cardiac arrest.

In conclusion, in this study early mortality was highly frequent in COVID-19 patients, accounting for nearly half of all deaths. Early deaths were not explained by differences in age, sex and comorbidities compared with late deaths. However, patients with early mortality arrived with a more severe disease at hospital admission. We believe that the frequency and causes of early mortality in COVID-19 should be monitored. This approach would aid the evaluation and optimization of educational strategies for the population, support the calls for early medical care and outpatient monitoring, and help in the organisation of the primary care response, since SARS-CoV-2 will continue to cause disease in the coming months.

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