

# Clinical features and their association with death in a large cohort of adult inpatients with COVID-19

## Características clínicas y su asociación con la muerte en una gran cohorte de pacientes adultos hospitalizados con COVID-19

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### ABSTRACT

**Objective:** To determine the clinical features and their association with death in a large cohort of adult inpatients with COVID-19.

**Material and Methods:** Retrospective cohort study of patients admitted by COVID-19 to the Almenara General Hospital in Lima, Peru, between March and May 2020. Clinical features on admission were evaluated according to death in bivariate and multivariate Cox regression analyses.

**Results:** A total of 533 patients were included (23% women; 55% over 60 years-old; 27% death). Those who died had significantly higher proportions of patients over 60 years, pre-existing diseases, and severe/critical illness compared to alive patients: 73% vs. 44%,  $p < 0.001$ ; 68% vs. 57%,  $p = 0.021$ ; and 46%/34% vs. 28%/16%,  $p < 0.001$ , respectively. In bivariate analyses age over 60 years (uHR 2.49, 95%CI: 1.83-3.39), atrial fibrillation (uHR 2.09, 95%CI: 1.03-4.24) and hypothyroidism (uHR 2.75, 95%CI: 1.02-7.45) were associated with death. While in the multivariate analyses age over 60 years (aHR 2.53, 95%CI: 1.81-3.53), obesity (aHR 2.43, 95%CI: 1.44-4.07), chronic renal disease (aHR 2.65, 95%CI: 1.21-5.82) and hypothyroidism (aHR 4.22, 95%CI: 1.47-12.1) were independently associated with higher risk of death.

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**Conclusions:** During the first two months of the epidemic, patients admitted by COVID-19 at the Almenara General Hospital were more frequently older men and had a relevant pre-existing disease burden, as well as severe and critical illness. Mortality was high and was associated with older age, obesity, chronic renal disease, and hypothyroidism.

**Keywords:** COVID-19; inpatients; risk factors; death; cohort study (source: MeSH-NLM).

## RESUMEN

**Objetivo:** Determinar las características clínicas y su asociación con muerte en una gran cohorte de pacientes adultos hospitalizados por COVID-19.

**Materiales y Métodos:** Estudio de cohorte retrospectivo con pacientes admitidos por COVID-19 en el Hospital General Almenara de Lima, Perú, entre marzo y mayo 2020. Las características clínicas al momento de la admisión fueron evaluadas de acuerdo con el desenlace de muerte en un análisis bivariado y multivariado con el modelo de regresión de Cox.

**Resultados:** Un total de 533 pacientes fueron incluidos (23% mujeres; 55% mayores de 60 años de edad; 27% de letalidad). Entre quienes murieron hubo significativamente mayores proporciones de personas mayores de 60 años, enfermedades preexistentes y enfermedades graves o críticas comparado con quienes permanecieron vivos: 73% vs. 44%,  $p < 0.001$ ; 68% vs. 57%,  $p = 0.021$ ; y 46%/34% vs. 28%/16%,  $p < 0.001$ , respectivamente. En el análisis bivariado edad mayor de 60 años (HRc 2.49, IC95%: 1.83-3.39), fibrilación auricular (HRc 2.09, IC95%: 1.03-4.24) e hipotiroidismo (HRc 2.75, IC95%: 1.02-7.45) fueron asociados con muerte. En el análisis multivariado edad mayor a 60 años (HRa 2.53, IC95%: 1.81-3.53), obesidad (HRa 2.43, IC95%: 1.44-4.07), enfermedad renal crónica (HRa 2.65, IC95%: 1.21-5.82) e hipotiroidismo (HRa 4.22, IC95%: 1.47-12.1) fueron asociados independientemente con mayor riesgo de muerte.

**Conclusiones:** Durante los dos primeros meses de la epidemia, los pacientes admitidos por COVID-19 en el Hospital General Almenara fueron más frecuentemente hombres adultos mayores con una carga de enfermedad preexistente relevante, así como con enfermedad grave o crítica. La letalidad fue alta y se asoció con edad avanzada, obesidad, enfermedad renal crónica e hipotiroidismo.

**Palabras clave:** COVID-19; pacientes internos; factores de riesgo; muerte; estudios de cohortes (fuente: DeCS-BIREME).

## INTRODUCTION

The Americas have become one of the epicentres of the COVID-19 pandemic in the world. But not only that, several countries on the continent, including our own, are among those with the most confirmed cases and deaths in the world<sup>1</sup>. Therefore, it is important to know the clinical behaviour of COVID-19 in these countries.

Multiple studies addressed the clinical features and outcomes of COVID-19 patients; however, the vast majority have done so with small case series, with less than one hundred patients<sup>2-8</sup>, or intermediate series, with a number of patients between one and three hundred<sup>9-15</sup>. Few studies in the world have characterized the clinical features and outcomes in larger hospital cohorts.

To this end, a study was conducted at the Guillermo Almenara Irigoyen National Hospital (Almenara Hospital), one of the three main general hospitals of the Social Security Health Care System in Metropolitan Lima. We evaluated the clinical features and their association with death in patients during the first two months of COVID-19 pandemic.

## MATERIAL AND METHODS

We performed a retrospective cohort study of all patients with etiological evidence of COVID-19 admitted to the Almenara Hospital Emergency Room between March 15 and May 14, 2020. Etiological evidence for COVID-19

was obtained by reverse transcription-polymerase chain reaction (RT-PCR) on nasal and pharyngeal swab samples and by rapid antibody test on the peripheral fingertip or venous blood. The RT-PCR tests were processed at the Peruvian National Institute of Health. The process also excluded patients with RT-PCR or rapid antibody tests that were negative for SARS-CoV-2. Finally, pregnant, or postpartum women and children were excluded, to make the study population less heterogeneous.

Clinical variables that were evaluated upon admission of patients to the emergency room were: age in years, sex, pre-existing disease (there was no specific operational definition, we considered the record that the doctors considered relevant), main symptom, severity according to World Health Organization<sup>16</sup>, clinical outcome (death versus alive), and hospital stay in days. As of May 31st, the outcome of the patients had occurred and been known in 96% of the cases. The remaining data were completed later. The analysis was done with descriptive statistics, chi-square or Fisher's exact test for proportions, and Student's "t" test for means. Later, to identify factors related to the outcome of death, bivariate and multivariate analysis was made with Cox's Proportional Risks model. The analysis was adjusted with clinical variables of interest. In addition, survival curve according oxygen saturation was elaborated. The R statistical software (version 1.2, www.r-project.org, R studio Inc., GNU Public License) was used for all

calculations.

Due to its importance and scope, it should be noted that it was a decision not to address in the same work aspects referred to laboratory tests and treatment. Thus, the present study focuses on carrying out an in-depth clinical analysis of COVID-19 and death in patients.

The study was promoted and authorized by the Coordination of the Emergency and Disaster Monitoring Space (EMED for its acronym in Spanish), and the Chair of the Emergency Department when the initial medical response to the epidemic was concentrated. Both positions were held by one of the authors (GED). The clinical data for the study were obtained from regularly collected electronic medical records of the patients. The confidentiality of their data was preserved.

## RESULTS

A total of 533 patients with etiological evidence of COVID-19 were included in the study. Evidence was obtained by RT-PCR test in 299 cases (56%) and by rapid antibody test in the remaining 234 cases (44%). On the other hand, 153 patients were excluded: 136 by negative diagnostic tests (102 rapid tests and 34 RT-PCR), nine

pregnant women and two postpartum women, and six children.

The clinical features of the patients according to their outcome are presented in Table 1. There were significant clinical differences in age, preexisting diseases, and severity of the disease among those who died and alive. In contrast, there were no significant clinical differences in terms of sex, type of evidence of disease, clinical presentation on admission, and mean length of hospital stay. It should be noted that severity was determined with oxygen saturation (obtained by pulse oximetry or arterial blood), inspired fraction of oxygen, or oxygen measured in arterial blood. Thus, those who died had higher proportions of severe and critical illness than those alive. Table 1.

Preexisting diseases to COVID-19 according to death are presented in Table 2. As can be seen, there were no statistically significant differences between those who died and those alive.

However, there was a marginally significant difference in the preexistence of atrial fibrillation (or other arrhythmias) and chronic renal disease. Those who died had higher proportions of atrial fibrillation and chronic kidney disease than those alive. Table 2.

**Table 1.** Clinical features of the patients according to their outcome

Variable	Total N = 533	Deceased N = 204	Alive N = 329	p Value
Age				
Mean [SD]	61 [15]	67 [13]	58 [15]	<0,001
Over 60 years old	294 [55]	148 [73]	146 [44]	<0,001
Sex				
Women	157 [29]	58 [28]	99 [30]	0,683
Men	376 [71]	146 [72]	230 [70]	
Diagnosis by				
RT-PCR	299 [56]	114 [56]	185 [56]	0,937
Quick test	234 [44]	90 [44]	144 [44]	
Pre-existing diseases				
None	200 [38]	64 [32]	136 [43]	0,021
One or more	333 [62]	140 [68]	193 [57]	
Main symptom				
Dyspnea	210 [39]	88 [43]	122 [37]	0,523*
Cough	178 [33]	66 [32]	112 [34]	
Fever	107 [20]	36 [18]	71 [22]	
Others	38 [8]	14 [7]	24 [7]	
Severity (WHO, N=509)				
Mild	62 [12]	11 [06]	51 [16]	<0,001
Moderated	152 [30]	27 [14]	125 [40]	
Severe	179 [35]	90 [46]	89 [28]	
Critical	116 [23]	66 [34]	50 [16]	
Length of hospital stay				
Mean [SD]	8,8 [9,8]	9,4 [8,3]	8,5 [10,6]	0,289

\* Fisher's exact test. SD, standard deviation

**Table 2.** Pre-existing diseases to COVID-19 according to the outcome

Pre-existing chronic diseases	Total N = 533	Deceased N = 204	Alive N = 329	p Value
Hypertension	167 [31]	71 [35]	96 [29]	0,174
Diabetes	117 [22]	42 [21]	75 [23]	0,549
Obesity	36 [6,8]	18 [8,8]	18 [5,5]	0,134
Hypothyroidism	8 [1,5]	4 [1,9]	4 [1,2]	0,717*
Chronic Kidney Disease	36 [6,8]	19 [9,3]	17 [5,2]	0,064
CKDV in haemodialysis	25 [4,7]	12 [5,9]	13 [3,9]	0,305
Bronco - Lung	30 [5,6]	12 [5,9]	18 [5,5]	0,841
Asthma	17 [3,2]	9 [4,4]	8 [2,4]	0,310*
Interstitial fibrosis	3 [0,6]	2 [0,9]	1 [0,3]	0,561*
Tuberculosis**	9 [1,7]	2 [0,9]	7 [2,1]	0,493*
Hearts	16 [3,0]	8 [3,9]	8 [2,4]	0,434*
Atrial fibrillation	12 [2,3]	8 [3,9]	4 [1,2]	0,067*
Heart failure	1 [0,2]	1 [0,5]	0 [0,0]	0,383*
Coronary disease	2 [0,4]	0 [0,0]	2 [0,6]	0,527*
Malignant neoplasms	8 [1,5]	4 [1,9]	4 [1,2]	0,717*
Hematologic	1 [0,2]	1 [0,5]	0 [0,0]	0,383*
Solid organ	7 [1,3]	3 [1,5]	4 [1,2]	1,000*
Neurological - encephalic	5 [0,9]	2 [0,9]	3 [0,9]	1,000*
Parkinson	3 [0,6]	0 [0,0]	3 [0,9]	0,290*
Cirrhosis	3 [0,6]	2 [0,9]	1 [0,3]	0,561*
HIV/AIDS	4 [0,8]	1 [0,5]	3 [0,9]	0,664*
Psoriasis	3 [0,6]	2 [0,9]	1 [0,3]	0,561*
Psychiatric	4 [0,8]	1 [0,5]	3 [0,9]	0,664*

Frequencies reported as n [%];\* Fisher exact test; \*\* As a background.

**Table 3.** Bivariate and multivariate analyses of factors associated with mortality

Variables	Bivariate uHR [CI95%]	Multivariate <sup>a</sup> aHR [CI95%]
Age (over 60 years old)	2,49 [1,83-3,39]***	2,53 [1,81-3,53]***
Sex (male)	0,92 [0,68-1,25]	0,97 [0,69-1,35]
Hypertension	1,15 [0,86-1,53]	0,99 [0,71-1,37]
Diabetes	0,85 [0,61-1,20]	0,93 [0,64-1,33]
Obesity	1,43 [0,88-2,33]	2,43 [1,44-4,07]***
Hypothyroidism	2,75 [1,02-7,45]*	4,22 [1,47-12,1]**
Chronic kidney disease	0,99 [0,62-1,59]	2,65 [1,21-5,82]*
CKD 5 <sup>b</sup>	0,77 [0,43-1,39]	0,32 [0,12-0,87]*
Asthma	1,22 [0,62-2,40]	1,52 [0,73-2,81]
Atrial fibrillation	2,09 [1,03-4,24]*	1,61 [0,78-3,34]
Malignant neoplasm	1,77 [0,65-4,77]	2,14 [0,77-5,93]
Cirrhosis	1,60 [0,40-6,44]	1,78 [0,43-7,32]
HIV <sup>c</sup> disease	1,35 [0,33-5,44]	0,90 [0,21-3,75]
Severity <sup>d</sup>		
Moderate	0,65 [0,32-1,31]	0,57 [0,28-1,19]
Severe	1,41 [0,75-2,67]	1,31 [0,70-2,60]
Critical	1,56 [0,82-2,97]	1,43 [0,68-2,54]

uHR, unadjusted Hazard Ratio; aHR, adjusted Hazard Ratio. <sup>a</sup> Conducted in 509 cases with available data on severity, events: 194. <sup>b</sup> Stage 5 chronic kidney disease on regular dialysis. <sup>c</sup> Human Immunodeficiency Virus. <sup>d</sup> Reference mild severity \* p<0,05; \*\* p<0,01; \*\*\*p<0,001

Table 3 presents results of bivariate and multivariate analysis. In the first only age over 60 years, atrial fibrillation and hypothyroidism were associated with death. While in the second age over 60 years, obesity, chronic renal disease, and hypothyroidism were independently associated with higher risk of death. A secondary analysis

of ambient oxygen saturation levels vs. death is showing in Table 4. The unadjusted analysis was performed on 406 patients with available data on ambient oxygen saturation. According to it, patients with oxygen saturation less than or equal to 70%, with a critical level, presented a significantly higher risk of death.

**Table 4.** Unadjusted association between oxygen saturation and mortality

Oxygen saturation	uHR [CI95%] <sup>a</sup>	p Value
More or equal 95% and 100%	Reference	
From 94% to more than 90%	0,63 [0,30-1,33]	0,223
Less than or equal to 90% to more than 70%	1,16 [0,62-2,19]	0,644
Less than or equal to 70%	3,26 [1,58-6,72]	0,001

<sup>a</sup> N = 406; events = 140; uHR, unadjusted Hazard Ratio.

**Table 5.** Clinical data compared with published studies

Features	Collins JA	Mejia F (17)	Li X (18)	Feng Y (19)	Cai Q (20)	Goyal P (21)	Perez P (22)
Country	Peru	Peru	China	China	China	USA	UK
City	Lima	Lima	Wuhan	Three provinces	Shenzhen	New York	London
Establishment	HNGA <sup>a</sup>	HNCH <sup>b</sup>	Hosp. Tongji <sup>c</sup>	Three <sup>d</sup>	TPHS <sup>e</sup>	Two <sup>f</sup>	Three <sup>g</sup>
Population	N = 533	N = 369	N = 548	N = 476	N = 383	N = 393	N = 614
Published in	In progress	2020 Dec 28	2020 Jul	2020 Jun 1	2020 Jul	2020 Jun 11	2021 Dec 6
Admission period (in 2020)	Mar 15 to May 14	Mar 29 to ---	Jan 26 to Feb 5	Jan 1 to Feb 15	Jan 11 to Feb 21	Mar 3 to 27	Feb 25 to Apr 5
Censored (in 2020)	Jul 31	Jun 11	Mar 3	Mar 21	Mar 26	Apr 10	May 1st
Standard cohort	Retrospective	Retrospective	Retrospective	Retrospective	Retrospective	Retrospective	Retrospective
Age							
Median [IQR]	62 [51-73]	59 [49-68]	60 [48-69]	53 [40-64]	44 y 61 <sup>h</sup>	62 [49-74]	69 [25]
> 60 years [%]	55	50	38 <sup>i</sup>	25 <sup>i</sup>	---	---	---
Sex [%]							
Female	29	35	49	43	52	39	38
Male	71	65	51	57	48	61	62
<b>Pre-existing chronic diseases</b>							
	<b>N = 533</b>	<b>N = 369</b>	<b>N = 548</b>	<b>N = 476</b>	<b>N = 383</b>	<b>N = 393</b>	<b>N = 614</b>
Grouped, %							
One or more	62	69	---	43	---	---	78
None	38	31	---	57	---	---	22
Individuals, %							
Hypertension	31	22	30	28	15	50	47
Diabetes	22	22	15	10	5,7	25	35
Obesity	6,8	42	--- <sup>i</sup>	---	11 <sup>j</sup>	36 <sup>k</sup>	--- <sup>j</sup>
Hypothyroidism	1,5	---	---	---	---	---	---
Chronic kidney disease	6,8	2,0	1,8	0,8	---	4,6 <sup>l</sup>	17
Bronco - lung diseases							
Asthma	3,2	6,5	0,9	---	---	12,5	9,1
COPD	0,4	1,0	3,1	4,6	8,4	5,1	4,9



Interstitial fibrosis	0,6	0,8	---	---	---	---	---
Tuberculosis*	1,7	4,0	1,6	---	---	---	---
<b>Heart diseases</b>							
Atrial fibrillation	2,3	---	---	---	---	---	12
Heart failure	0,2	0,5	---	---	---	---	6,0
Coronary disease	0,4	1,6	6,2	8,0 <sup>m</sup>	9,1 <sup>m</sup>	14	13
<b>Malignant neoplasm</b>							
Hematologic	0,2	---	---	---	---	---	1,3
Solid organ	1,3	---	---	---	---	---	9,6
Cerebrovascular disease	0,0	---	---	3,6	---	---	9,3
Cirrhosis	0,6	0,3	---	---	5,2 <sup>n</sup>	1,5	2,1
HIV / AIDS o ID <sup>***</sup>	0,8	0,3	---	1,5	---	1,8	1,5
Psoriasis	0,6	---	---	---	---	---	---
<b>Symptoms</b>	<b>N = 533</b>	<b>N = 369</b>	<b>N = 548</b>	<b>N = 476</b>	<b>N = 383</b>	<b>N = 393</b>	<b>N = 614</b>
Dyspnoea	39	---	57	24	---	56	65
Cough	33	---	76	59	39	79	74
Sputum production	---	---	---	36	---	---	---
Fever	20	15 <sup>o</sup>	95	86	70	77 <sup>p</sup>	82
Chills	---	---	---	---	---	---	---
Odynophagia	2,1	---	51	8,1	1,0	---	---
Asthenia / fatigue	0,6	---	47	---	4,2	---	---
Headache	1,7	---	11	---	2,1	---	---
Myalgia	0,6	---	20	13	---	27	---
Diarrhoea	0,2	---	33	11 <sup>q</sup>	2,9	24	32 <sup>q</sup>
Vomiting	---	---	8,2	---	---	19	---
<b>Severity</b>							
Not severe	45	36	51	74	76	---	---
Severe / critical	55	64 <sup>r</sup>	49 <sup>s</sup>	26 <sup>t</sup>	24	---	---
<b>Outcome</b>							
Death	38	50	16 <sup>u</sup>	8	0,8	10	29
Alive	62	50	53	85	---	66	62
Hospitalized	0	0	31 <sup>v</sup>	7	---	24	9
<b>Length of hospital stay</b>							
Median [IQR]	6 [3-12]	7 [3-10]	---	16 [12-24]	22-34 <sup>w</sup>	---	7 [6-8]

<sup>a</sup> Hospital Nacional Guillermo Almenara Irigoyen– EsSalud; <sup>b</sup> Hospital Nacional Cayetano Heredia – Minsa; <sup>c</sup> Sino-French New City Branch of Tongji Hospital, Huazhong University of Science and Technology in Wuhan, Hubei Province; <sup>d</sup> Third People's Hospital of Shenzhen (in Canton Province), Jinyintan Hospital (in Wuhan, Hubei Province) and Shanghai Public Health Clinical (in Shanghai); <sup>e</sup> Tongling People's Hospital in Anhui Province (<http://govt.chinadaily.com.cn/a/201904/19/W55cde9e4b498e079e68021237.html>); <sup>f</sup> New York - Presbyterian Hospital's Weill Cornell Medical Center and Lower Manhattan Hospital (<https://www.nyp.org/about-us>); <sup>g</sup> Three hospitals of Imperial College Healthcare NHS Trust (<https://www.imperial.nhs.uk/>); <sup>h</sup> Median in non-severe and severe patients, respectively (the study does not present the median as a total population); <sup>i</sup> the median of body mass index (BMI) in the total population was 25 in the study by Li X, et al and 28 in that by Perez PN, et al; but they do not indicate the percentages of obesity; <sup>j</sup> Obesity if BMI > 28; the study had 32% overweight (BMI > 24 and < 28); <sup>k</sup> If BMI > 30; <sup>l</sup> Cases of stage V chronic kidney disease; <sup>m</sup> Percentages referred to cardiovascular disease; <sup>n</sup> Referred to as prevalent liver disease; <sup>o</sup> Temp. > 38 °C on admission; <sup>p</sup> Temp. > 38 °C on access in 26% of cases; <sup>q</sup> not only as diarrhoea but as a digestive symptom; <sup>r</sup> based on oxygenation parameters reported in the article; <sup>s</sup> according to IDSA; <sup>t</sup> according to CURB-65; <sup>u</sup> data with 545 patients; <sup>v</sup> with 32 days of follow-up. Median range.

\* As background, \*\* Atrial fibrillation, and other arrhythmias, \*\*\* Other immunodeficiencies.

## DISCUSSION

Our study presents the largest cohort nationally and one of the largest internationally with the clinical features and their association with death of adult inpatients with COVID-19 in a national general hospital. The study was mainly composed of older male adults with a significant preexisting disease burden. Likewise, most were admitted with a severe and critical illness. And the outcome was fatal in four out of ten patients, independently associated with age, obesity, chronic kidney disease, and hypothyroidism. We compared our clinical data with that of published studies similar to ours both in population size and in the level of care of the health care facility (Table 5). The comparison includes another study realized in Peru<sup>17</sup>, three in China<sup>18,19,20</sup>, one in US<sup>21</sup> and one in UK<sup>22</sup>. These studies include cohorts with more than 300 inpatients. In general, the best epidemiological and clinical profile of adult inpatients with COVID-19 was that of China, while London and New York were the worst. Ours is in an intermediate position, except for the patients' outcome in which the Lima studies present the worst results. These variations may reflect cultural and demographic differences and the availability of resources for the clinical support of patients.

Age is an independent factor with death, consistently<sup>17,18,19,23,24</sup>. In this line, the risk of dying in the present study was two and a half times greater in patients over 60 years of age than in those under this age.

The variability in the prevalence of preexisting diseases to COVID-19 is important (Table 5, 2nd part). The most notorious occurred with obesity. Four of the six cohorts with whom ours is compared used the Quetelet body mass index, but only two indicated the percentage of obesity<sup>20,21</sup>. One of them focuses precisely on the effect of this variable. The study used the body mass index for the diagnosis of overweight and obesity, with results adjusted for Asia<sup>20</sup>. In the other three studies, it is assumed that the registration of obesity was a clinical observation product at the time of patient admission. In the present study, we took the data in this way, consistent with the low percentage of obesity. Even so, it was sufficient to constitute an independent factor of death. With the advent of the epidemic of COVID-19, obesity has been identified as an independent risk factor for severity and worse prognosis<sup>20,23,25,26</sup>. In these studies, the independent risk of obesity compared to those with a normal body mass index was two or three times higher. In New York<sup>21</sup>, the patients who most frequently received ventilatory support were male and obese.

Chronic kidney disease is another significant disease because of its relative frequency and because it is an independent factor of death, as defined in this study, consistent with others<sup>22,23</sup>. Interestingly, the subgroup of patients in haemodialysis that is easy to identify had protective factor behaviour.

On the other hand, hypothyroidism is a significant chronic disease in the general population because of its frequency rather than its severity. As far as we know, this is the first

study that includes hypothyroidism in the relationship of preexisting chronic conditions to COVID-19. But not only that, this is also the first study to show such an entity as an independent factor of death, even though its management has not represented a particular concern during the pandemic<sup>27</sup>. In contrast, the prevalence of hyperthyroidism as a preexisting condition was much lower than that of hypothyroidism. However, the occurrence of this condition in inpatients with COVID-19 may be high (20%, 58/287)<sup>28</sup>. Thus, thyroid disease should be present in the evaluation of inpatients with COVID-19 both on admission as a pre-existing condition and in the evolution as an occurrence, given that this is a systemic disease.

The severity of COVID-19 is important because it is a significant determinant of death, which seems to become more evident when the ambient oxygen saturation level falls to a critical level below 70%. Virtually six out of ten patients were admitted with severe and acute illness to our centre, in contrast to one to three out of ten patients in China. The percentage of severe and critical cases was even higher than ours in another local study<sup>17</sup>. Late patient attendance at hospitals may be one explanation for the differences. Still, it may also reflect cultural differences and the organization of the state (and country) response, in general, and the national health system, in particular.

A similar contrast with China is observed when evaluating the hospital mortality of COVID-19, which is closely related to the severity with which patients are admitted. However, the higher lethality in the other local study<sup>17</sup> would have other explanations, which go through the resources available to support patients' treatment. This same argument would explain a lower lethality in New York<sup>21</sup> and London<sup>22</sup> concerning our centre. It is important to note that the overall study's overall lethality most double that found in a systematic review of only older adult patients with COVID-19<sup>29</sup> (38% vs. 20%, respectively). However, the older patients' lethality in the present study is even higher (50% vs. 20%, respectively), which highlights the importance of adopting or implementing appropriate preventive measures and the best support strategies with fewer or more resources available to assist this vulnerable population.

Although the focus of the study is not therapeutic, we must indicate that patients received oxygen via low-flow nasal cannula or reservoir mask. During the first wave of COVID-19 we did not have high flow nasal prongs for oxygen. While serious or critical patients went to the intensive care unit - COVID-19 according to the priorities established by this area.

The main limitation of the study has to do with the retrospective collection of clinical data at entry. The same occurred with the data on the outcome and hospital stay, although in these cases the data were unambiguous. The study's strengths are its size; the complete data on the clinical outcome of the patients admitted and the performance of an analysis compared with studies of similar size. This provides a better approach to the reality



of patients in clinical practice.

In conclusion, the adult inpatients with COVID-19 at the Almenara Hospital in the first two months of the epidemic in our country were predominantly older men with a significant burden of pre-existing diseases. The most frequent clinical features upon admission were dyspnoea, cough, and fever, with a predominance of severe and critical illness. Lethality was high, and the hospital stay was short. Factors independently associated with lethality were age over 60 years, obesity, chronic renal disease, and hypothyroidism.

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