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Characteristics, complications and outcomes among 1549 patients hospitalised with COVID-19 in a secondary hospital in Madrid, Spain: a retrospective case series study

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ABSTRACT

Objectives To describe demographic, clinical, radiological and laboratory characteristics, as well as outcomes, of patients admitted for COVID-19 in a secondary hospital.

Design and setting Retrospective case series of sequentially hospitalised patients with confirmed SARS-CoV-2, at Infanta Leonor University Hospital (ILUH) in Madrid, Spain.

Participants All patients attended at ILUH testing positive to reverse transcriptase-PCR on nasopharyngeal swabs and diagnosed with COVID-19 between 1 March 2020 and 28 May 2020.

Results A total of 1549 COVID-19 cases were included (median age 69 years (IQR 55.0–81.0), 57.5% men). 78.2% had at least one underlying comorbidity, the most frequent was hypertension (55.8%). Most frequent symptoms at presentation were fever (75.3%), cough (65.7%) and dyspnoea (58.1%). 81 (5.8%) patients were admitted to the intensive care unit (ICU) (median age 62 years (IQR 51–71); 74.1% men; median length of stay 9 days (IQR 5–19)) 82.7% of them needed invasive ventilation support. 1393 patients had an outcome at the end of the study period (case fatality ratio: 21.2% (296/1393)). The independent factors associated with fatality (OR; 95% CI): age (1.07; 1.06 to 1.09), male sex (2.86; 1.85 to 4.50), neurological disease (1.93; 1.19 to 3.13), chronic kidney disease (2.83; 1.40 to 5.71) and neoplasia (4.29; 2.40 to 7.67). The percentage of hospital beds occupied with COVID-19 almost doubled (702/361), with the number of patients in ICU quadrupling its capacity (32/8). Median length of stay was 9 days (IQR 6–14).

Conclusions This study provides clinical characteristics, complications and outcomes of patients with COVID-19 admitted to a European secondary hospital. Fatal outcomes were similar to those reported by hospitals with a higher level of complexity.

Strengths and limitations of this study

- ► This is a large retrospective case series study of 1549 sequentially hospitalised patients with confirmed SARS-CoV-2.
- ► The study describes the response of a secondary hospital based in a region of Spain with the highest incidence of COVID-19, and how the hospital was transformed into a centre entirely dedicated to COVID-19.
- ► A complete follow-up was made of all patients during hospital stay, although after discharge no outcome information was collected, so only in-hospital fatality could be estimated.

BACKGROUND

In December 2019, a novel coronavirus (SARS-CoV-2) emerged in China and spread globally, causing a new infectious disease named 'COVID-19'.[1] By 28 May 2020, the epidemic reaches 5 593 631 confirmed cases and more than 353 334 deaths across 216 countries all over the world.[2]

The first confirmed case of COVID-19 in Spain was reported from La Gomera (Canary Islands) on 31 January 2020.[3] But it was not until the last week of February 2020 when the first five cases were reported in the community of Madrid.[4]

During March and April 2020 (first COVID-19 wave in Spain and Europe), Spain had been one of the most affected countries by the coronavirus, being one of the main outbreaks of the disease worldwide. Spain is now the second country in Europe with the highest number of confirmed cases (after the

Russian Federation) with 470 973 cases as of 1 September 2020.[2 5 6] The rate of infections in the community of Madrid has exceeded every other region in Spain, with more than 27% of all confirmed cases in Spain and an accumulated number of 45 074 hospitalised patients and 8662 deaths as of 1 September 2020.[5]

Hospitals of the various regional health services of Spain are categorised into different complexity levels depending on their size, technological resources and the higher or lower availability of different clinical departments, thus, in ascending order of complexity we have primary, secondary and tertiary level hospitals; tertiary hospitals often have specific clinical departments that attend patients coming from different parts of the country. The Infanta Leonor University Hospital (ILUH) is a secondary level hospital with 361 beds, including 8 in the intensive care unit (ICU). It serves the population of Vallecas (305 262 individuals).[7] Our healthcare area has a disproportionate number of beds per inhabitants: 1.07 beds per 1000 people compared with 2.15 beds per 1000 people overall within the region. Vallecas is one of the COVID-19 most affected areas in the city of Madrid (Spain) with 9947 total confirmed COVID-19 cases as of 1 September 2020.[8] Therefore, the level of hospital saturation during the epidemy has been one of the greatest in Spain. As a consequence, the hospital was in March transformed into a centre entirely dedicated to COVID-19 and all its professionals focused on assisting patients affected by the SARS-CoV-2 infection.

Limited information is available to describe characteristics, complications and mortality in COVID-19 overloaded secondary Spanish hospitals. The available data from Spain refer to tertiary hospitals, multicentric studies or primary care settings.[9–12]

This study describes the clinical characteristics, severity, types of treatments and overall outcomes of patients with confirmed SARS-CoV-2 infection admitted to ILUH in Madrid (Spain).

METHODS

Study design and participants

A single-centre retrospective observational study that included patients attended at ILUH with a laboratory-confirmed COVID-19 between 1 March 2020 and 28 May 2020. SARS-CoV-2 infection was confirmed by real-time reverse transcriptase-PCR (RT-PCR) assay (FTD SARS-CoV-2 Assay by SIEMENS) from nasopharyngeal swabs (Deltaswab by Deltalab). Patients discharged from the emergency department and those transferred to another hospital in the first 48 hours were not included in the final analysis; although these patients were hospitalised at ILUH, they did not stay enough time to record all the relevant clinical data due to the hospital overcapacity context. Once selected patients that met inclusion criteria, no one was excluded.

Epidemiological and demographic data, medical history, baseline comorbidities, symptoms and signs both at admission and during follow-up, laboratory findings, RT-PCR results, treatment strategy used for COVID-19, complications and survival data were obtained from patient's electronic medical records. All-cause mortality was calculated including deaths occurred both in patients pending admission (first 48 hours) and during hospitalisation. ICU admission, hospitalisation, length of stay and ventilatory support (invasive mechanical ventilation, non-invasive mechanical ventilation or oxygen mask) were also registered. Different time intervals were calculated: lag time between symptoms onset and diagnosis, length of stay at ICU and overall length of stay at the hospital.

Data were collected and managed using REDCap (Research Electronic Data Capture) electronic data capture tools hosted at Ideas for Health Association. REDCap is a secure, web-based software platform designed to support data capture for research studies.[13]

The Strengthening the Reporting of Observational Studies in Epidemiology statement guidelines were followed in the conduct and reporting of the study (see online supplemental file).

Patient and public involvement

There was no patient or public involvement in the development of the research design or in conducting the study.

Statistical analysis

A descriptive analysis of the clinical background and baseline characteristics of the patients was performed. Continuous variables are presented as median and IQR, after testing normal distribution. Categorical variables are expressed as number of patients and percentage. Two age groups were defined using a cut-off value of 65 (<65 and ≥65 years old) for the comparison of the clinical characteristics of the cohort. For the ICU analysis, the comparison of the characteristics between admitted and non-admitted to ICU patients was limited to patients under 65 years because age was one of the major criteria for a better allocation of ICU resources in a context of limited availability of them.

For the mortality analysis, the case fatality ratio (CFR) was defined as number of deaths of patients with laboratory-confirmed COVID-19 divided by the number of laboratory-confirmed COVID-19 cases admitted to the hospital. The outcomes were defined as death or recovered, and the clinical characteristics between these groups were compared using X^2 test for the categorical variables and median test for the quantitative variables.

Logistic regression analysis was carried out to ascertain the effect of sociodemographic and clinical background characteristics on mortality. Variables that showed statistical significance ($p<0.05$) in the univariate analysis and clinical variables that could have potential relevance on the outcome according to the current available evidence were included in the model. OR and 95% CIs were calculated.

Statistical analyses were done using Stata software (V.14.0; Stata Corporation, College Station, Texas, USA).

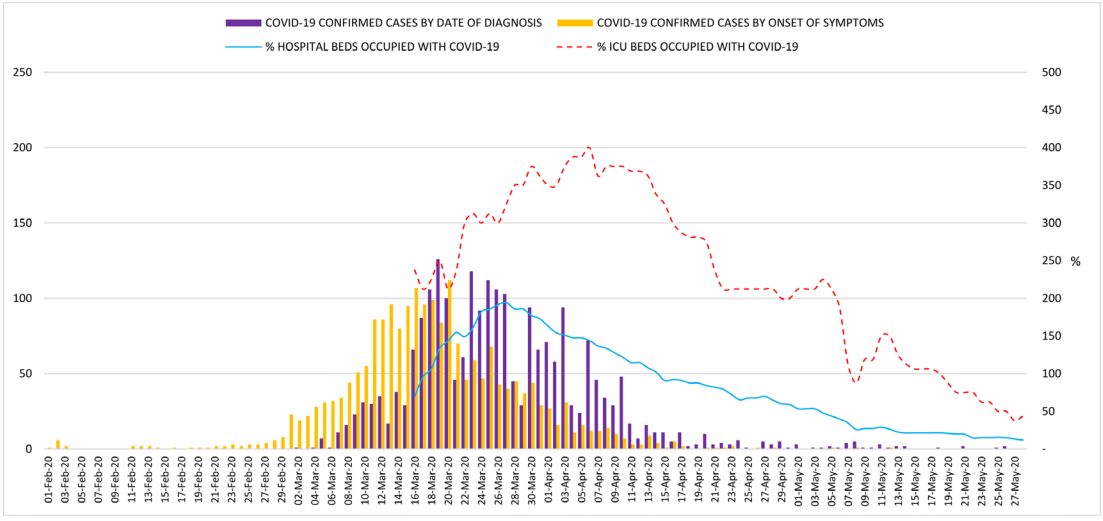

Figure 1 Epidemic curve of COVID-19 confirmed cases seen at ILUH. ILUH, Infanta Leonor University Hospital.

RESULTS

Overall, 2259 COVID-19 confirmed cases were attended at ILUH during the study period. The daily number of confirmed COVID-19 cases are plotted by the date of diagnosis (date of positive RT-PCR) and by the date of symptoms onset in figure 1. The first positive patient in our hospital was diagnosed on 1 March 2020 and the epidemic curve peaked on 19 March when 126 PCR tested positive. From that date, the incidence declined gradually but it took over a month to have a daily number of new cases below 10. The percentage of ICU beds and total hospital beds occupied with patients with COVID-19 are shown in figure 1. On 27 March, our hospital almost doubled its bed capacity with 702 hospitalised patients. On 6 April, 32 patients were in ICU, reaching 400% of hospital ICU capacity.

Among these 2259 patients, we analysed 1549 cases and excluded 710 because they were discharged from the emergency department or transferred to other hospitals in the first 48 hours. For the complications, ICU and mortality analysis, 156 patients with an incomplete episode were excluded because they were transferred to other hospitals during their stay or were still hospitalised by 28 May 2020 (figure 2).

Age range of the 1549 hospitalised patients varied from 3 weeks to 102 years old, median was 69 (IQR 55.0–81.0), and 57.5% were men. All patients except for the 3-week-old baby were adults. Of these, 55.0%

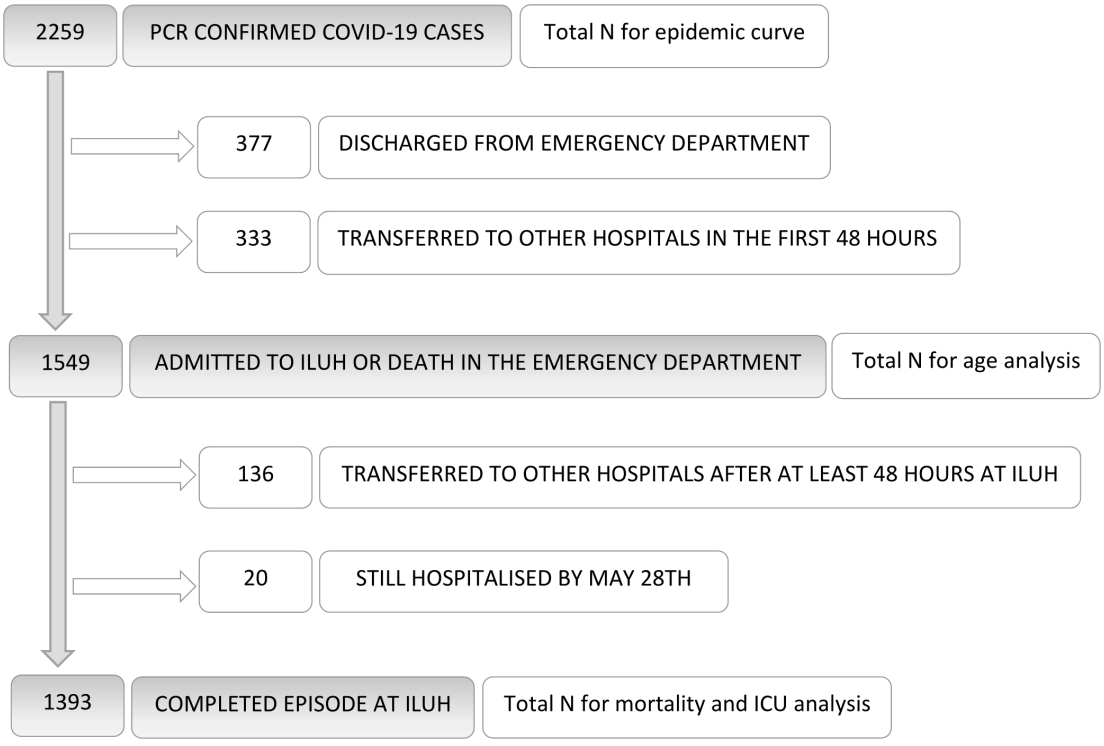

Figure 2 Population flow chart. ICU, intensive care unit; ILUH, Infanta Leonor University Hospital.

Table 1 Clinical characteristics and treatment (N=1549)

	Overall	<65 years old	≥65 years old	
	n/N (%)	n/N (%)	n/N (%)	P value
Male	890/1549 (57.5)	400/642 (62.3)	490/907 (54.0)	0.001
Migrant	385/1549 (24.8)	296/642 (46.1)	89/642 (13.9)	<0.001
Clinical background				
Influenza vaccine 19/20	498/1101 (45.2)	90/463 (19.4)	408/638 (63.9)	<0.001
Cardiological disease	375/1545 (24.3)	37/640 (5.8)	338/905 (37.3)	<0.001
High blood pressure	851/1548 (55.0)	185/641 (28.9)	666/907 (73.4)	<0.001
Diabetes mellitus	382/1541 (24.8)	85/636 (13.4)	297/905 (32.8)	<0.001
Tobacco smoker/ex-smoker	374/1344 (27.8)	121/555 (21.8)	253/789 (32.0)	<0.001
Obesity	240/1531 (15.7)	110/636 (17.3)	130/895 (14.5)	0.129
COPD	211/1541 (13.7)	37/638 (5.8)	174/903 (19.3)	<0.001
Asthma	122/1545 (7.9)	51/639 (8.0)	71/906 (7.8)	0.668
OSAS	79/935 (8.4)	32/401 (8.0)	47/534 (8.8)	0.654
Cerebrovascular disease	57/125 (45.6)	12/28 (42.7)	45/97 (46.4)	0.741
Thromboembolic disease	41/939 (4.4)	10/410 (2.4)	31/529 (5.9)	0.011
Neurological disease	178/1540 (11.6)	37/637 (5.8)	141/903 (15.6)	<0.001
Chronic kidney disease	104/1543 (6.7)	16/639 (2.5)	88/904 (9.7)	<0.001
Cirrhosis	28/1540 (1.8)	13/638 (2.0)	15/902 (1.7)	0.209
Haematological/oncological cancer	103/1540 (6.7)	21/640 (3.3)	82/900 (9.1)	<0.001
HIV	9/1542 (0.6)	7/639 (1.1)	2/903 (0.2)	0.012
Autoimmune disease	47/913 (5.1)	17/393 (4.3)	30/520 (5.8)	0.328
Symptoms				
Fever	1159/1540 (75.3)	533/638 (83.5)	626/902 (69.4)	<0.001
Headache	133/1533 (8.7)	92/634 (14.5)	41/899 (4.6)	<0.001
Malaise	671/1533 (43.8)	282/637 (44.3)	389/896 (43.3)	0.928
Confused	87/1532 (5.7)	11/633 (1.7)	76/899 (8.4)	<0.001
Dyspnoea	891/1533 (58.1)	362/632 (57.3)	529/901 (58.7)	0.382
Superior respiratory tract symptoms	316/1534 (20.6)	153/635 (24.1)	163/899 (18.1)	0.009
Cough	1010/1538 (65.7)	469/638 (73.5)	541/900 (60.1)	<0.001
Expectoration	194/1535 (12.6)	69/635 (10.9)	125/900 (13.9)	0.167
Haemoptysis	26/1532 (1.7)	15/633 (2.3)	11/899 (1.2)	0.207
Chest pain	134/1534 (8.7)	79/635 (12.4)	55/899 (6.1)	<0.001
Muscle pain	291/1534 (19.0)	166/635 (26.1)	125/899 (13.9)	<0.001
Abdominal pain	49/1534 (3.19)	16/635 (2.52)	33/899 (3.67)	0.280
Nausea/vomiting	178/1532 (11.6)	88/636 (13.8)	90/896 (10.0)	0.040
Diarrhoea	269/1530 (17.6)	143/636 (22.5)	126/894 (14.1)	<0.001
Skin rash	8/1531 (0.5)	5/636 (0.8)	3/895 (0.3)	0.087
Anosmia	41/1153 (3.6)	29/489 (5.9)	12/664 (1.8)	<0.001
Complications during admission				
Bacterial pneumonia	43/1362 (3.2)	13/551 (2.4)	30/811 (3.7)	0.320
Sepsis	28/1372 (2.0)	16/554 (2.9)	12/818 (1.5)	0.054
Respiratory distress syndrome	195/1368 (14.2)	74/550 (13.4)	121/818 (14.8)	0.557
Pneumothorax	5/1373 (0.4)	3/556 (0.5)	2/817 (0.2)	0.488
Pleural effusion	29/1367 (2.1)	6/552 (1.1)	23/815 (2.8)	0.032
Stroke	11/1373 (0.8)	4/555 (0.7)	7/818 (0.9)	0.669
Disseminated intravascular coagulation	9/1369 (0.7)	2/554 (0.4)	7/815 (0.9)	0.360
Thrombosis	55/824 (6.7)	23/338 (6.8)	32/486 (6.6)	0.833
Acute renal failure	165/1373 (12.0)	37/556 (6.6)	128/817 (15.7)	<0.001

Continued

Table 1 Continued

	Overall	<65 years old	≥65 years old	
	n/N (%)	n/N (%)	n/N (%)	P value
Treatment				
HCQ monotherapy	28/1549 (1.8)	7/642 (1.1)	21/907 (2.3)	0.075
HCQ+AZ	927/1549 (59.8)	448/642 (69.8)	479/907 (52.8)	<0.001
HCQ+LP/r	98/1549 (6.3)	32/642 (5.0)	66/907 (7.3)	<0.001
HCQ+AZ+LP/r	287/1549 (18.5)	90/642 (14.0)	197/907 (21.7)	<0.001
HCQ+LP/r+IFN-b	37/1549 (2.4)	12/642 (1.9)	25/907 (2.8)	0.260
HCQ+AZ+LP/r+IFN-b	113/1549 (7.3)	37/642 (5.8)	76/907 (8.4)	0.051
Tocilizumab	240/1549 (15.5)	144/642 (22.4)	96/907 (10.6)	<0.001
Corticosteroids	684/1549 (44.2)	264/642 (41.1)	420/907 (46.3)	<0.001

AZ, azithromicine; COPD, chronic obstructive pulmonary disease; HCQ, hydroxicloroquine; IFN-b, interferon-beta; LP/r, lopinavir-ritonavir; OSAS, obstructive sleep apnoea syndrome.

had hypertension, 24.8% diabetes, 24.3% cardiovascular disease, 15.7% obesity, 13.7% chronic obstructive pulmonary disease (COPD) and 8.5% obstructive sleep apnoea syndrome (OSAS). HIV infection (0.6%) and autoimmune disease (5.2%) were rare. Overall, 1221 (78.2%) patients had at least one underlying comorbidity.

The median lag time between symptoms onset and diagnosis was 7 days (IQR: 4–9) (figure 1). The most common symptoms at presentation were fever (75.3%), cough (65.7%) and dyspnoea (58.1%). Diarrhoea (17.6%) and anosmia (3.6%) were less common in our case series. Fever, headache, cough, diarrhoea, nausea/vomiting, anosmia, muscle or chest pain were more frequent in younger patients while cognitive deterioration was in older patients (table 1).

The most frequent therapies used for treating COVID-19 were the combination hydroxychloroquine plus azithromycin (59.9%) and the combination hydroxychloroquine plus azithromycin plus lopinavir-ritonavir (18.5%). Any treatment combination including lopinavir-ritonavir was more frequently used in older patients. Tocilizumab was used in 15.5% of the patients and corticosteroids in 44.2% (table 1).

The analysis of the complications during admission showed that 14.3% of patients had acute respiratory distress syndrome with no differences between age groups, 12.0% had acute kidney failure which was more frequent in older patients (15.7% vs 6.7%), 6.7% had a clinical thrombotic event and 0.7% had disseminated intravascular coagulation (table 1).

Among patients with a complete episode at ILUH, 81 were admitted to ICU: median age 62 (IQR 51–71); 74.1% men; median length of stay 9 days (IQR 5–19) and 82.7% of them needed invasive ventilation support. Clinical characteristics are shown in table 2. Among the 575 patients younger than 65 years old with a complete episode at ILUH, risk factors associated to ICU admission in the univariate analysis were: being men, obesity, hypertension, OSAS, high respiratory rate, a low blood oxygen saturation level at admission, a high neutrophil/lymphocyte ratio, an elevated plasma international normalised ratio, lactate dehydrogenase, aspartate transaminase, creatinine and C reactive protein and the presence of alveolar pulmonary infiltrates in the chest X-ray (table 2). We calculated CFR in ICU patients with a complete episode at ILUH (70 patients): global CFR was 72.9% (62.8% in the under 65 group and 88.9% in the older group).

The overall CFR in our cohort was 21.2% (296/1393 cases). The median length of stay was 9 days (IQR 6–14). Among the 296 deaths, 48 occurred in the first 48 hours and the rest during hospitalisation. These 48 patients had a higher median age compared with the global cohort (82.5 vs 69) and their median lag time from symptom onset until fatality was lower (7 days vs 13.5 days, p<0.001). As shown in table 3, patients who died were older and more likely to be men, current smoker/ex-smoker, and had hypertension, cardiovascular disease, COPD, OSAS, diabetes mellitus, neurological disease, chronic kidney disease and neoplasia in the univariate analysis. Also, they received more frequently ventilatory support during hospitalisation and showed more alveolar pulmonary infiltrates in chest X-ray than people who recovered.

In the multivariate analysis, independent factors related to death were: years of age (OR 1.07; 95% CI: 1.06 to 1.09), being men (OR 2.86; 95% CI: 1.85 to 4.50), neurological disease (OR 1.93; 95% CI: 1.19 to 3.13), chronic kidney disease (OR 2.83; 95% CI: 1.40 to 5.71) and neoplasia (OR 4.29; 95% CI: 2.40 to 7.67).

Among the 1549 hospitalised patients, 65 were readmitted (4.2%): 64.6% were men and 67.7% were 65 years old or older. CFR during readmissions was 10.8% (7/65).

DISCUSSION

This study describes the COVID-19 series of a secondary level hospital in Madrid, Spain.

During the outbreak, hospital wards almost doubled their capacity (702/361), with the number of patients in ICU quadrupling its capacity (32/8). Beds were brought from other hospitals (antique not working hospitals) to turn single rooms into double rooms and to make surge beds in large waiting room areas, which became ward beds. A cohort system (confirmed cases located together

Table 2 Clinical, laboratory and diagnosis imaging characteristics of patients with COVID-19 who have been admitted in ICU

		<65-year-old patients (n=575)		
	ICU patients cohort (n=81)	Admitted to ICU (n=50)	Non-admitted to ICU (n=525)	P value
Age*	62 (51–71) (N=81)	54 (48–60) (N=50)	53 (45–59) (N=525)	0.625
Male†	60/81 (74.1)	21/50 (42.0)	325/525 (61.9)	0.048
Migrant†	25/81 (30.9)	21/50 (42.0)	238/525 (45.3)	0.651
Influenza vaccine 19/20†	12/42 (28.6)	5/28 (17.9)	75/395 (19.0)	0.883
Clinical background				
Cardiovascular disease†	17/81 (21.0)	6/50 (12.0)	29/523 (5.5)	0.069
High blood pressure†	43/81 (53.1)	23/50 (46.0)	147/524 (28.1)	0.008
Diabetes mellitus†	23/81 (28.4)	10/50 (20.0)	65/519 (12.5)	0.315
Tobacco smoker/ex-smoker†	23/76 (30.3)	13/49 (26.5)	98/450 (21.8)	0.447
Obesity†	23/81 (28.4)	17/50 (34.0)	80/520 (15.4)	0.001
COPD†	7/81 (8.6)	4/50 (8.0)	30/521 (5.8)	0.522
Asthma†	5/81 (6.2)	4/50 (8.0)	43/522 (8.2)	0.117
OSAS†	8/39 (20.5)	8/27 (29.6)	22/332 (6.6)	<0.001
Thromboembolic disease†	2/40 (5.0)	2/28 (7.1)	8/338 (2.4)	0.136
Neurological disease†	5/80 (6.3)	2/49 (4.1)	31/521 (6.0)	0.786
Chronic kidney disease†	5/81 (6.2)	3/50 (6.0)	12/522 (2.3)	0.118
Liver cirrhosis†	1/80 (1.3)	1/50 (2.0)	11/522 (2.1)	0.117
Haematological/oncological cancer†	4/81 (4.9)	1/50 (2.0)	19/523 (3.6)	0.548
HIV†	0/81 (0.0)	0/50 (0.0)	7/522 (1.3)	0.529
Clinical and laboratory presentation				
Heart rate (beats per minute)*	94 (83–107) (N=73)	54 (48–60) (N=50)	53 (45–59) (N=525)	0.625
Respiratory rate (breaths per minute)*	23 (18–30) (N=44)	24 (18–30) (N=33)	18 (16–20) (N=222)	0.002
Systolic blood pressure (mm Hg)*	133 (119–142) (N=66)	128 (118–141) (N=42)	125 (114–137) (N=292)	0.591
SpO2 (%)*	88 (76–93) (N=69)	88 (66–94) (N=44)	96 (92–97) (N=454)	<0.001
SpO2 <90%†	39/81 (48.1)	26/50 (52.0)	53/525 (10.1)	<0.001
SpO2 after oxygen administration (%)*	95 (90–97) (N=39)	95 (90–98) (N=27)	96 (94–98) (N=91)	0.813
SpO2 <90% after oxygen administration†	9/81 (11.1)	5/50 (10.0)	0/525 (0.0)	<0.001
Haemoglobin (g/L)*	13.9 (11.9–15.0) (N=81)	14.1 (12.1–15.2) (N=50)	14.1 (13.1–15.1) (N=493)	0.946
Neutrophils (cells count/µL)*	6300 (4500–9300) (N=81)	7000 (4600–8800) (N=50)	4700 (3500–6700) (N=495)	0.001
Lymphocytes (cells count/µL)*	900 (600–1200) (N=81)	900 (700–1300) (N=50)	1100 (800–1400) (N=495)	0.252
Neutrophil/lymphocyte ratio*	6.64 (5.0–12.7) (N=81)	6.69 (4.8–12.3) (N=50)	4.4 (2.9–7.1) (N=495)	<0.001
Platelets ($\times 10^9$/L)*	209 (170–267) (N=81)	205 (172–265) (N=50)	213 (171–274) (N=495)	0.777
INR*	1.1 (1.0–1.2) (N=81)	1.1 (1.0–1.2) (N=50)	1.1 (1.0–1.1) (N=484)	0.035
D-dimer (mg/L)*	940 (485–2095) (N=56)	790 (470–2350) (N=35)	640 (400–1080) (N=334)	0.163
LDH (U/L)*	408 (279–542) (N=70)	415 (279–605) (N=43)	271 (215–348) (N=430)	<0.001
ALT (U/L)*	45 (32–67) (N=80)	50 (34–80) (N=50)	44 (30–66) (N=494)	0.075
AST (U/L)*	59 (40–82) (N=79)	60 (43–85) (N=50)	40 (29–57) (N=485)	<0.001
Creatinine (mg/dL)*	1.1 (0.9–1.3) (N=78)	1.1 (1.0–1.3) (N=48)	0.9 (0.7–1.1) (N=480)	<0.001
C reactive protein (mg/L)*	1157 (481–2054) (N=80)	1234 (678–2133) (N=49)	522 (174–1152) (N=494)	<0.001
Diagnosis imaging				
Bilateral pulmonary infiltrates†	61/74 (82.4)	40/46 (87.0)	388/476 (81.5)	0.359
Interstitial pulmonary infiltrates†	61/81 (75.3)	38/50 (76.0)	360/525 (68.6)	0.277
Alveolar pulmonary infiltrates†	51/81 (63.0)	33/50 (66.0)	230/525 (43.8)	0.003
Respiratory supplementation				

Continued

Table 2 Continued

		<65-year-old patients (n=575)		
	ICU patients cohort (n=81)	Admitted to ICU (n=50)	Non-admitted to ICU (n=525)	P value
Oxygen therapy†	77/81 (95.1)	47/50 (94.0)	345/516 (66.9)	<0.001
Non-invasive ventilation†	38/80 (47.5)	26/49 (53.1)	25/513 (4.9)	<0.001
Invasive ventilation†	67/81 (82.7)	43/50 (86.0)	0/514 (0.0)	<0.001

Comparison between patients under 65 years of age admitted to ICU versus non-admitted to ICU.
*Continuous variable (median, IQR, N)
†Categorical variables (n/N, %)
ALT, alanine aminotransferase; AST, aspartate transaminase; COPD, chronic obstructive pulmonary disease; ICU, intensive care unit; INR, international normalised ratio; LDH, lactate dehydrogenase; OSAS, obstructive sleep apnoea syndrome; SpO2, partial oxygen saturation.

and patients with similar suspect degree too) was followed during the early stages of the epidemic in order to avoid hospital transmission. Some weeks after the beginning of the pandemic, the gym used for patient's rehabilitation was transformed into a semicritical unit where patients discharged from the ICU or patients needing closer monitoring or high-flow oxygen were admitted. The ordinary activity in consultations and elective surgery was cancelled, the paediatric emergencies were referred to other hospitals and all doctors attended patients with COVID-19 exclusively. All physicians and nursing staff were organised into two groups: the COVID-19 assistance group, led by the internal medicine department: they attended patients with COVID-19; and the COVID-19 non-assistance group which gave all the administrative support: requesting laboratory tests, writing clinical reports, informing about clinical evolution to patient's relatives and so on. Regarding critical care beds: our hospital regular capacity comprises eight beds for ICU and six for the surgical critical care. Surge critical care beds were made available in the post-anaesthesia care unit (6 beds) and the outpatient surgery post-anaesthesia care unit (12 beds), to a maximum of 32 critical care beds.

Patients' baseline characteristics were similar to the largest published series in Spain,[10] although our patients were older and with a higher proportion of men compared with other tertiary Spanish hospital series.[9]

We found that younger patients showed a high incidence of fever, cough, headache, muscle pain and diarrhoea, whereas older patients showed a less specific clinical presentation. Other studies did not find differences in clinical presentation related to age.[14] This information could be crucial for the rapid identification and isolation of the suspected cases at any healthcare level.

Our cohort showed a high incidence of acute kidney failure during hospitalisation similar to other non-Spanish series[15 16] but higher than other Madrid series,[9] with no association to drug administration. This could be explained for the rapid hydroelectrolytic imbalance in older patients in the context of an acute systemic viral disease. We also found a high incidence of thrombotic events (6.7%) comparable with previous reports,[17] although disseminated intravascular coagulation was rare.

Lopinavir/ritonavir-based treatments were more frequently used in older patients. This finding is due to the use of this drug as standard treatment in our hospital protocol during the first half of the outbreak, when most of the patients were older than 65 years. Tocilizumab, with or without corticosteroids, was used following Spanish Drug Agency recommendations in patients who developed cytokine release storm which is believed to cause acute respiratory distress syndrome, although corticosteroids were also used in other clinical contexts.

During the study, criteria for ICU admission was the need for mechanical ventilation. Due to the number of ICU beds made available for the number of patients admitted to hospital, which doubled the usual hospital capacity, during the study period 22 patients were transferred to other ICUs of Madrid, to make ILUH's ICU beds available for other patients. In the same way, due to the scarce ICU bed capacity, triage of patients had to be done. The selection for ICU admission opportunity was made individually, based on each patient's comorbidities, functional capacity, age (never solely age as a criteria) and depending on the availability of critical care beds at the moment. A local guideline for patient admission on critical care unit was made, based on the consensus document released by the Spanish Society of Intensive and Critical Care and other 17 medical societies.[18] On the other hand, non-invasive mechanical ventilation or high-flow oxygen, managed by pneumologists, was available in the ward for selected patients not admitted to ICU.

Our findings in the ICU analysis in patients under 65 years old were analogous to other studies[16 19 20] in terms of clinical characteristics and laboratory values. As described in the New York series,[16] it seems that obesity and OSAS were related factors leading to ICU admission, even more than the presence of a previous pulmonary disease. This could suggest that patients with a baseline ventilatory compromise could entail a higher risk for ICU admission due to alveolar hypoventilation and acute-on-chronic hypercapnic respiratory failure. However, this analysis has some limitations related to scarce availability of ICU resources in our centre and the number of ICU patients who were transferred to other hospitals.

The CFR in our series was 21.2%. It has probably been overestimated due to a significant proportion of patients

Table 3 Clinical, laboratory and diagnosis imaging characteristics of patients with COVID-19 who died or recovered

	Death (n=296)	Recovered (n=1097)	P value
Age*	82 (71.5–87) (N=246)	65 (53–78) (N=1097)	<0.001
Male†	208/296 (70.3)	593/1097 (54.1)	<0.001
Migrant†	41/296 (13.8)	296/1097 (27.0)	<0.001
Clinical background			
Influenza vaccine 19/20†	113/183 (61.7)	342/820 (41.7)	<0.001
Cardiovascular disease†	124/296 (41.9)	217/1093 (19.8)	<0.001
High blood pressure†	208/296 (70.3)	565/1096 (51.5)	<0.001
Diabetes mellitus†	90/295 (30.5)	260/1090 (23.8)	0.038
Tobacco smoker/ex-smoker†	111/260 (42.7)	236/950 (23.8)	<0.001
Obesity†	42/292 (14.4)	169/1085 (15.6)	0.169
COPD†	67/293 (22.9)	120/1092 (11.0)	<0.001
Asthma†	17/296 (5.7)	95/1093 (8.7)	0.166
OSAS†	20/156 (12.8)	53/687 (7.7)	0.041
Thromboembolic disease†	11/161 (6.8)	26/681 (3.8)	0.093
Neurological disease†	59/293 (20.1)	101/1091 (9.3)	<0.001
Chronic kidney disease†	40/295 (13.6)	58/1092 (5.3)	<0.001
Liver cirrhosis†	8/292 (2.7)	17/1093 (1.5)	0.352
Haematological/oncological cancer†	48/293 (16.4)	50/1092 (4.6)	<0.001
HIV†	0/295 (0.0)	8/1091 (0.7)	0.327
Clinical and laboratory presentation			
Heart rate (beats per minute)*	88 (78–102) (N=242)	88 (78–100) (N=881)	0.856
Respiratory rate (breaths per minute)*	21.5 (16–28) (N=116)	18 (16–20.5) (N=397)	<0.001
Systolic blood pressure (mm Hg)*	130 (111–147) (N=217)	130 (117–143) (N=683)	0.877
SpO2 (%)*	89 (82–93) (N=239)	95 (92–97) (N=945)	0.033
SpO2 <90%†	121/203 (59.6)	152/945 (16.1)	<0.001
SpO2 after oxygen administration (%)*	94 (90.5–97) (N=112)	96 (94–98) (N=203)	0.003
SpO2 <90% after oxygen administration†	18/112 (16.1)	7/203 (0.1)	<0.001
Haemoglobin (g/L)*	12.70 (11.00–14.50) (N=292)	13.70 (12.60–14.70) (N=1054)	<0.001
Neutrophils (cells count/µL)*	6100 (4200–8550) (N=292)	4800 (3500–6800) (N=1057)	<0.001
Lymphocytes (cells count/µL)*	800 (500–1100) (N=292)	1000 (800–1300) (N=1057)	<0.001
Neutrophil/lymphocyte ratio*	7.17 (4.3–12.9) (N=292)	4.67 (3.1–7.4) (N=1057)	<0.001
Platelets ($\times 10^9$/L)*	190 (142.5–263.5) (N=292)	209 (162–273) (N=1057)	0.040
INR*	1.1 (1.0–1.3) (N=283)	1.1 (1.0–1.2) (N=1026)	<0.001
D-dimer (mg/L)*	1060 (570–2560) (N=167)	750 (450–1330) (N=685)	<0.001
LDH (U/L)*	345 (249–479) (N=235)	259 (210–331) (N=887)	<0.001
ALT (U/L)*	31 (23–47) (N=287)	36 (25–55) (N=1050)	<0.001
AST (U/L)*	47 (30–67) (N=284)	38 (28–55) (N=1035)	<0.001
Creatinine (mg/dL)*	1.2 (0.9–1.7) (N=285)	0.9 (0.7–1.2) (N=1032)	<0.001
C reactive protein (mg/L)*	105.9 (36.2–182.4) (N=291)	53.8 (18.3–111.4)	<0.001
Diagnosis imaging			
Bilateral pulmonary infiltrates†	218/259 (84.2)	762/960 (79.4)	0.084
Interstitial pulmonary infiltrates†	182/296 (61.5)	689/1097 (62.8)	0.677
Alveolar pulmonary infiltrates†	153/296 (51.7)	458/1097 (41.7)	0.002
Respiratory supplementation			
Oxygen therapy†	285/292 (97.6)	458/1075 (76.5)	0.001
Non-invasive ventilation†	57/289 (19.7)	64/1072 (6.0)	<0.001
Invasive ventilation†	46/292 (15.7)	15/1075 (1.4)	<0.001

*Continuous variable (median, IQR, N)
†Categorical variable (n/N, %)
ALT, alanine aminotransferase; AST, aspartate transaminase; COPD, chronic obstructive pulmonary disease; INR, international normalised ratio; LDH, lactate dehydrogenase; OSAS, obstructive sleep apnoea syndrome; SpO2, partial oxygen saturation.

transferred to other hospitals in the first 48 hours, who had a less severe disease. Some published series showed a lower CFR,[21] although others reported a similar[9 10 16] or even higher CFR.[15 22] The differences could be related to demographic factors, different hospital admission criteria, case definition and healthcare system overload level.[23] It is interesting to note that the CFR found in our study is similar to other Spanish tertiary level hospitals,[9] despite our sample had a higher proportion of older and male patients and our centre had a lower proportion of conventional hospitalisation and ICU beds availability. The CFR in our ICU was slightly lower than other studies.[16] Our CFR similar to other hospitals with greater capacity could be related to a better reorganisation of spaces and resources. Some areas of the hospital were reoriented to attend patients with COVID-19 like paediatric or anaesthesia areas. Comparing the patients who died in the first 48 hours (48/296) with the rest of the deceased, the median age was higher and the median days from symptom onset until fatality were lower. This could reflect a steep clinical deterioration in older patients compared with younger patients. Further studies are required to support the evidence of a severe clinical phenotype of SARS-CoV-2 infection characterised by a quick progression of an acute respiratory failure with severe hypoxemia in older patients that leads to fatal outcome.

We found similarities with other series[24] about variables associated to fatality in the univariate analysis, such as hypertension, cardiovascular disease or pulmonary diseases. Nevertheless, after adjusting by sociodemographic variables and comorbidities at admission, risk factors related to death were age, male gender, neurological disease, chronic kidney disease and cancer. These findings are consistent with other studies that identify male sex and age as important predictors for mortality.[25] However, this analysis has some limitations because it only focuses on hospitalised patients skewing estimates of the morbi-mortality and risk factors of COVID-19 globally.[11]

The strength of this study lies on the sequential collection of patients (all patients with COVID-19 admitted to hospital were included) and on the complete follow-up of all patients during their entire hospital stay. On the other hand, it also has some limitations. First, its observational and retrospective nature. Second, some variables (ie, anosmia and history of thromboembolic event) have a relatively large number of missing values because they were not registered from the beginning of the study, due to changes in the evidence related to COVID-19 during the progression of the pandemic. Third, there is no follow-up after hospital discharge, so only in-hospital fatality can be estimated.

We are now attending a second outbreak of COVID-19 in Madrid. Compared with the first outbreak, the speed of community transmission is lower, the case detection capacity is higher, there is more knowledge of the disease and the possible treatments and healthcare settings are better prepared. All these factors will probably have a great impact on the analysis if the study were to be repeated now. Future analysis comparing results from first and consecutive waves of COVID-19 pandemic at ILUH would be interesting to make.

CONCLUSION

This study describes the epidemic progression, clinical characteristics, complications and outcomes of patients with COVID-19 attended in a secondary level hospital in one of the highest COVID-19 incidence neighbourhoods of Madrid, which turned into an entire COVID-19 centre and almost doubled its bed capacity, during the first wave of COVID-19 pandemic in Spain. Fatal outcomes were similar to those reported by hospitals with a higher level of complexity.

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Competing interests None declared.

Patient consent for publication Not required.

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Characteristics, Complications and Outcomes Among 2259 Patients Hospitalized with COVID-19 in a Secondary Level Hospital in Madrid, Spain

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	***Yes*** ***Pag 1-2***
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	***Yes*** ***Pag 1-2***
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	***Yes*** ***Pag 3-4***
Objectives	3	State specific objectives, including any prespecified hypotheses	***Yes*** ***Pag 4***
Methods			
Study design	4	Present key elements of study design early in the paper	***Yes*** ***Pag 5***
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	***Yes*** ***Pag 5***
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	***Yes*** ***Pag 5***
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	***Yes*** ***Pag 5-6***
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	***Yes*** ***Pag 5-6***
Bias	9	Describe any efforts to address potential sources of bias	***Yes*** ***Pag 5-6***
Study size	10	Explain how the study size was arrived at	***Yes*** ***Pag 6***
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	***Yes*** ***Pag 6***

Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	***Yes*** ***Pag 6***
		(*b*) Describe any methods used to examine subgroups and interactions	***Yes*** ***Pag 6***
		(*c*) Explain how missing data were addressed	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	***Yes*** ***Pag 7***
		(b) Give reasons for non-participation at each stage	***Yes*** ***Fig 2***
		(c) Consider use of a flow diagram	***Yes*** ***Fig 2***
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	***Yes*** ***Pag 7-10*** ***Fig 1*** ***Tables 1-3***
		(b) Indicate number of participants with missing data for each variable of interest	***Yes*** ***Tables 1-3***
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	***Yes*** ***Pag 9*** ***Fig 1***
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	***Yes*** ***Pag 9*** ***Table 3***
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	***Yes*** ***Pag 7-10*** ***Tables 1-3***
		(*b*) Report category boundaries when continuous variables were categorized	***Yes*** ***Pag 7-10*** ***Tables 1-3***
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	***Yes*** ***Pag 9*** ***Uni/multivariate***
Discussion			
Key results	18	Summarise key results with reference to study objectives	***Yes*** ***Pag 10-12***
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	***Yes*** ***Pag 10-12***
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	***Yes*** ***Pag 10-12***
Generalisability	21	Discuss the generalisability (external validity) of the study results	***Yes*** ***Pag 12***

Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	***Yes*** ***Pag 14***

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.