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# The first 100 cases of COVID-19 in a Hospital in Madrid with a 2-month follow-up

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## ABSTRACT

**Background.** There are few descriptions of the clinical presentation and evolution of consecutive SARS-CoV-2 infections with a long-enough follow up.

**Methods.** Description of the first consecutive 100 patients with microbiologically-proven COVID-19 in a large hospital in Madrid, Spain including a minimum of two-month follow up.

**Results.** The median age of the patients (52% males) was 61.5 years (IQR=39.5-82.0) and the median BMI was 28.8 kg/m$^2$ (IQR=24.7-33.7). Overall 72% of the patients had one or more co-morbid conditions with a median age-adjusted Charlson index of 2 (IQR=0-5.7). Five patients (5%) were immunosuppressed. The most common symptoms at the time of diagnosis were fever (80.0%), cough (53.0%) and dyspnea (23.0%). The median $O_2$ saturation at the time of first examination was 94% (IQR=90-97). Chest X-ray on admission was compatible with pneumonia in 63% of the cases (bilateral in 42% and unilateral in 21%). Overall, 30% were managed at home and 70% were admitted to the hospital. Thirteen patients were admitted to the ICU with a median of 11 days of stay in the Unit (IQR=6.0-28.0). CALL score of our population ranged from 4 to 13. Overall, 60.0% of patients received antibiotic treatment and 66.0%, empirical antiviral treatment, mainly with lopinavir/ritonavir (65%) or hydroxychloroquine (42%). Mortality, with a minimum of 60 days of follow up, was 23%. The median age of the deceased patients was 85 years (IQR=79-93).

**Conclusions.** We found a high mortality in the first 100 patients diagnosed with COVID-19 at our institution, associated with advanced age and the presence of serious underlying diseases.

**Keywords: SARS-CoV-2, COVID-19, Coronavirus**

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## Los primeros 100 casos de COVID-19 en un Hospital de Madrid con seguimiento de 2 meses

## RESUMEN

**Antecedentes.** Existen pocas descripciones de la presentación clínica y evolución de infecciones consecutivas por SARS-CoV-2 con un seguimiento lo suficientemente largo.

**Métodos.** Descripción de los primeros 100 pacientes consecutivos con COVID-19 probada microbiológicamente en un gran hospital de Madrid, incluyendo un seguimiento mínimo de dos meses.

**Resultados.** La mediana de edad de los pacientes (52% hombres) fue de 61,5 años (RIC=39,5-82,0) y la mediana de IMC fue de 28,8 kg/m$^2$ (RIC=24,7-33,7). El 72% de los pacientes tuvieron una o más comorbilidades con un índice de Charlson ajustado a la edad de 2 (RIC=0-5,7). Cinco pacientes (5%) estaban inmunodeprimidos. Los síntomas más comunes al momento del diagnóstico fueron fiebre (80,0%), tos (53,0%) y disnea (23,0%). La mediana de saturación de $O_2$ en el momento del primer examen fue del 94% (RIC=90-97). La radiografía de tórax al ingreso fue compatible con neumonía en el 63% de los casos (bilateral en el 42% y unilateral en el 21%). El 30% fueron manejados en su domicilio y el 70% ingresados en el hospital. Trece pacientes ingresaron en la UCI con una mediana de 11 días de estancia en la Unidad (RIC=6,0-28,0).

El score CALL de nuestra población varió de 4 a 13. En general, el 60,0% de los pacientes recibió tratamiento antibiótico y el 66,0%, tratamiento antiviral empírico, principalmente con lopinavir/ritonavir (65%) o hidroxicloroquina (42%). La mortalidad, con un mínimo de 60 días de seguimiento, fue del 23%. La mediana de edad de los pacientes fallecidos fue de 85 años (RIC=79-93).

**Conclusiones.** Encontramos una alta mortalidad en los primeros 100 pacientes diagnosticados con COVID-19 en nuestra institución, asociada con edad avanzada y presencia de enfermedades subyacentes graves.

**Palabras clave: SARS-CoV-2, COVID-19, Coronavirus**

## INTRODUCTION

The COVID-19 epidemic is yielding highly variable data on incidence, evolution and mortality from one report to another, largely because the populations described are not comparable. On the other hand, the rush to provide valid scientific information on the epidemic means that many reports are preliminary and do not offer a sufficiently comprehensive perspective on the evolution of patients [1-10].

The first case of COVID-19 was confirmed in the Community of Madrid on February 27th, 2020 in a 24-year-old patient who had recently travelled to northern Italy. On March 1st, 2020, our institution (Hospital General Universitario Gregorio Marañón - HGUGM) admitted the first confirmed case to the Center and within 10 days another 99 patients were diagnosed consecutively. During this period, the diagnosis of SARS-CoV-2 infection was offered exclusively to symptomatic patients.

The criteria for hospital admission was initially systematic but soon those who did not have severity criteria began to be treated at home.

Having these first 100 patients a follow-up of 60, or more days in all cases, our objective is to evaluate this first series, with a special perspective on its presentation, treatment, evolution, and mortality.

## MATERIAL AND METHODS

**Location of the study.** The Hospital General Universitario Gregorio Marañón is a general and reference hospital, linked to the Universidad Complutense, with 1,350 beds, serving a population of approximately 350,000 inhabitants in the southeast area of Madrid. The Centre performs highly complex surgery, attends to patients with malignant diseases of both solid and haematological organs, has a very active transplant programme and is a reference center for many diseases. The Clinical Microbiology and Infectious Diseases Service is a multidisciplinary unit with a long history of care, teaching and research.

**Type of study and population.** This is a single-centre retrospective observational study that includes the first 100 consecutive patients with a proven diagnosis of COVID-19 in the HGUGM since the beginning of the epidemic, with a minimum follow-up of 60 days after etiological confirmation.

**Procedures.** The diagnosis of COVID-19 was performed in all cases from nasopharyngeal samples by reverse transcriptase polymerase chain reaction (Roche/Thermo Fisher RT-PCR) with prior extraction of viral RNA by NucliSENS® easyMag® (bioMérieux). A cycle threshold value (Ct-value) of less than 37 was considered positive. PCR (Roche/Thermo Fisher RT-PCR) from nasopharyngeal exudate was performed from the virus medium in which the samples are transported. The rest of the analytical determinations in blood followed the conventional methods established in our hospital.

**Data collected.** The following data were collected for each patient: demographic characteristics, underlying conditions, previous contact with suspected cases, days with symptoms prior to diagnosis by PCR, hospital stay, ICU stay, presence of pneumonia (unilateral/bilateral), oxygen saturation, laboratory analysis, severity of infection, antibiotic, antifungal and antiviral therapy, clinical evolution and mortality.

**Definitions.** Immunosuppressed patients were considered to be those with active solid organ tumor, malignant/hematological neoplasms under chemotherapy, HIV patients (<200 CD4), neutropenic individuals (<500 $mm^3$), solid organ transplant recipients or those under corticosteroid therapy at doses equivalent to ≥15 mg of prednisone (or equivalent)/day in the 30 days prior to admission.

Proven infection by SARS-CoV-2 was considered when a patient had signs and symptoms compatible with COVID-19 and a positive PCR in nasopharyngeal exudate.

The severity of the patients' disease was classified by the "CALL (comorbidity, age, lymphocyte and LDH) score" [11], which ranks 3 levels of risk according to their probability of progression. Those patients with 4-6 points have less than 10% chance of progression and are considered low risk (Class A). Patients with 7-9 points had a 10-40% chance of progression and are at intermediate risk (Class B) and patients with 10-13 points with more than 50% chance of progression are considered at high risk (Class C).

**Statistical analysis.** The median and interquartile range, were used for descriptive analysis of continuous variables. A value of $p<0.05$ was considered significant. Categorical variables were compared with the chi-square test and continuous variables using the Mann-Whitney test. A multivariate forward analysis including variables with $p<0.01$ in the univariate analysis was carried out to identify mortality risk factors. Statistical analysis was performed using IBM SPSS Statistics v.21 (IBM Corp., Armonk, NY).

**Ethical aspects.** This study was approved by the HGUGM Ethics Committee with the code MICRO.HGUGM.2020-020.

## RESULTS

Of the first 100 proven patients with COVID-19 at the HGUGM, 52% were male. The age of the patients ranged from

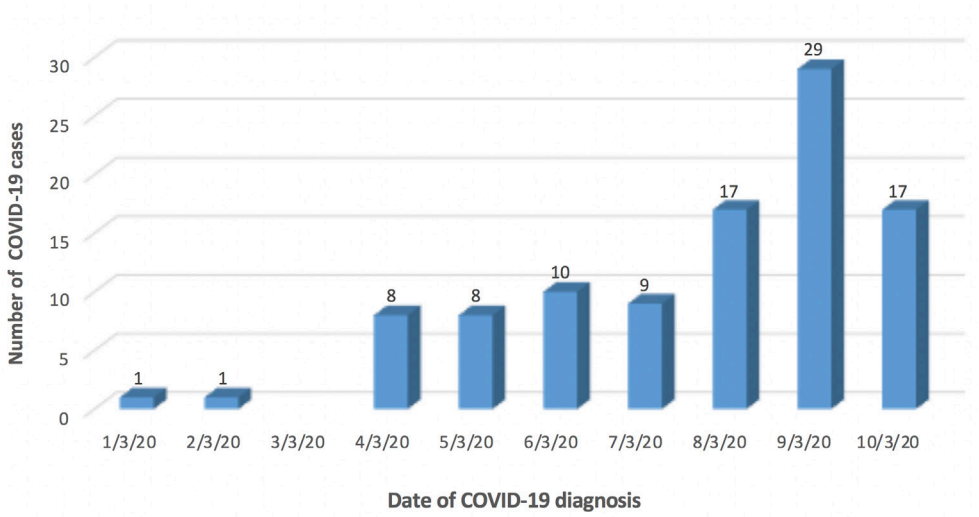


**Figure 1** Evolution of admissions of the first 100 cases with confirmed COVID-19 at Hospital General Universitario Gregorio Marañón.

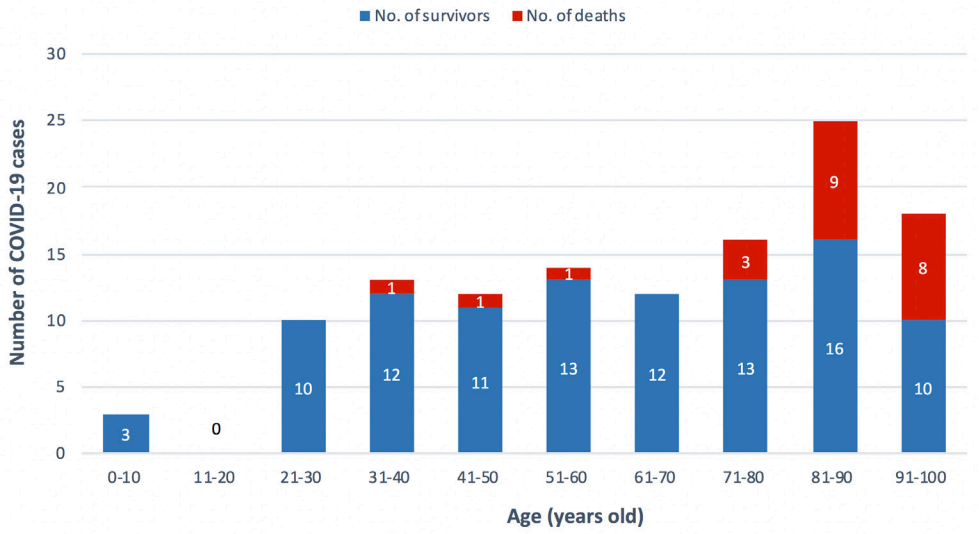


**Figure 2** Distribution of the first 100 COVID-19 cases (survivors/deaths) in the Hospital General Universitario Gregorio Marañón by decades of life.

3 months to 99 years with a median of 61.5 years (IQR=39.5-82.0). Figure 1 shows the speed at which the first 100 cases of COVID-19 were diagnosed in our institution and Figure 2 shows their distribution by decades of life and mortality rate.

The median patient weight was 75.8 kg (IQR=64.7-85.0) and the median Body Mass Index (BMI) was 28.8 kg/m$^2$ (IQR=24.7-33.7 kg/m$^2$). The characteristics of the patients and the main underlying diseases are shown in Table 1.

The most common comorbidities were hypertension (31%), heart disease (22%) and diabetes mellitus (19%). The age-adjusted Charlson index [12] ranged from a minimum of 0 to a maximum of 10 (median 2, IQR=0-5.7). Five patients (5%) were immunosuppressed. Twenty-eight percent of the patients had no underlying disease.

The most common symptoms presented by patients at the time of diagnosis were fever (80.0%), cough (53.0%) and dyspnea (23.0%), followed by myalgia (7.0%), chest discomfort (5.0%) and asthenia (4.0%) (Table 1). The median number of days patients referred symptoms prior to performing the diagnostic PCR of COVID-19 was 4.0 (IQR= 2.0-7.0) with a mini-

**Table 1** Demographic, clinical characteristics and evolution of patients.

| | Cases (n=100) |
|---|---|
| **Age,** median, IQR | 61.5 (39.5–82.0) |
| **Sex,** male, n (%) | 52 (52.0) |
| **BMI,** kg/m2 | 28.8 (24.7-33.7) |
| **Underlying diseases,** n (%) | |
| Cardiopathy | 22 (22.0) |
| Diabetes mellitus | 19 (19.0) |
| Malignant/Hematological neoplasia | 11 (11.0) |
| Chronic obstructive pulmonary disease | 10 (10.0) |
| Chronic renal disease | 8 (8.0) |
| Chronic hepatic disease | 7 (7.0) |
| Neurologic disease | 6 (6.0) |
| Solid tumor | 6 (6.0) |
| Psychiatric disease | 1 (1.0) |
| Hemodialysis | 0 |
| HIV | 0 |
| Solid organ trasplantation | 0 |
| **Other** | |
| Hypertension | 31 (31.0) |
| Hypothyroidism | 8 (8.0) |
| Asthma | 4 (4.0) |
| Cushing illness | 1 (1.0) |
| Celiac disease | 1 (1.0) |
| Lupus | 1 (1.0) |
| Sarcoidosis | 1 (1.0) |
| Myopathy | 1 (1.0) |
| Crohn disease | 1 (1.0) |
| Peptic esophagitis | 1 (1.0) |
| Osteoporosis | 1 (1.0) |
| Thyroiditis de Hashimoto | 1 (1.0) |
| Colon angiodysplasia | 1 (1.0) |
| Latent tuberculosis | 1 (1.0) |
| **None,** n (%) | 28 (28.0) |
| **Inmunodepressed,** n (%) | 5 (5.0) |
| **Charlson Index adjusted to age,** median, IQR | 2 (0-5.7) |
| Previous contact, n (%) | 47 (47.0) |
| Days with symptoms previous to PCR, median, IQR | 4.0 (2.0-7.0) |
| **Symptoms,** n, % | |
| Fever | 80 (80.0) |
| Cough | 53 (53.0) |
| Dyspnoea | 23 (23.0) |
| Myalgia | 7 (7.0) |
| Thoracic pain | 5 (5.0) |
| Asthenia | 4 (4.0) |

**Table 1** Demographic, clinical characteristics and evolution of patients (cont.)

| | Cases (n=100) |
|---|---|
| Headache | 3 (3.0) |
| Confusional syndrome | 3 (3.0) |
| Vomiting | 3 (3.0) |
| Diarrhea | 3 (3.0) |
| Dizziness | 2 (2.0) |
| Odinofagia | 2 (2.0) |
| Rhinorrea | 1 (1.0) |
| Conjunctivitis | 1 (1.0) |
| Pleuritic pain | 1 (1.0) |
| Syncope | 1 (1.0) |
| **Need of hospitalization,** n (%) | 70 (70.0) |
| Days of hospital stay, median, IQR | 9.0 (7.0-15.2) |
| **Need of ICU hospitalization,** n (%) | 13 (13.0) |
| Days of ICU stay, median, IQR | 11.0 (6.0-28.0) |
| **Pneumonia,** n (%) | 63 (63.0) |
| Unilateral pneumonia | 21 (21.0) |
| Bilateral pneumonia | 42 (42.0) |
| **Oxygen saturation** at hospital admission, median, IQR | 94.0 (90.0-97.0) |
| Lower level of **oxygen saturation** during hospitalization, median, IQR | 92.0 (88.0-94.0) |
| **Antiviral treatment,** n (%) | 66 (66.0) |
| **Antibiotic treatment,** n (%) | 60 (60.0) |
| **Antifungal treatment,** n (%) | 5 (5.0) |
| **Clinical outcome** at 30 days, alive, n (%) | 77 (77.0) |
| Recovered at home | 72 (72.0) |
| Hospitalized | 2 (2.0) |
| At ICU | 3 (3.0) |
| **Clinical outcome** at 60 days, alive, n (%) | 77 (77.0) |
| Recovered at home | 75 (75.0) |
| Hospitalized | 1 1.0) |
| At ICU | 2 (2.0) |
| **Mortality** | 23 (23.0) |
| Related to COVID | 22 (22.0) |
| Not related to COVID | 1 (1.0) |
| **Complications** | |
| Cardiopathy | 18 (18.0) |
| Acute respiratory distress syndrome | 30 (30.0) |
| Sepsis syndrome | 17 (17.0) |
| Proven bacterial sepsis | 9 (9.0) |
| Acute kidney injury | 27 (27.0) |
| Acute liver injury | 25 (25.0) |
| Pulmonary embolism | 1 (1.0) |

**Table 2** **Prognostic factors and clinical response to different treatments**

| | Total | Univariate analysis | | | Multivariate analysis | |
|---|---|---|---|---|---|---|
| | (n=100) | Survivor (n=77) | Non-survivor (n=23) | p | OR (95% CI) | p |
| **Age,** years, median (IQR) | 61.5 (39.5-82.0) | 54 (35.5-70.5) | 85.0 (79.0-93.0) | <0.01 | | |
| 0-18 | 3 (3.0) | 3 (3.9) | 0 (0) | 0.584 | | |
| 19-44 | 29 (29.0) | 28 (36.4) | 1 (4.3) | <0.01 | | |
| 45-54 | 11 (11.0) | 9 (11.7) | 2 (8.7) | 0.737 | | |
| 55-64 | 11 (11.0) | 11 (14.3) | 0 (0) | 0.064 | | |
| 65-74 | 11 (11.0) | 11 (14.3) | 0 (0) | 0.064 | | |
| ≥75 | 35 (35.0) | 15 (19.5) | 20 (87.0) | <0.01 | | |
| **Sex,** male, n (%) | 52 (52.0) | 41 (53.2) | 11 (47.8) | 0.812 | | |
| BMI, kg/m$^2$ | 28.8 (24.7-33.7) | 27.9 (24.4-30.5) | 30.8 (26.7-33.5) | 0.05 | | |
| BMI<30 | 42/69 (60.9) | 34/50 (68.0) | 8/19 (42.1) | 0.049 | | |
| BMI 30-40 | 24/69 (34.8) | 14/50 (28.0) | 10/19 (52.6) | 0.055 | | |
| BMI >40 | 3 /69 (4.3) | 2/50 (4.0) | 1/19 (5.3) | 0.818 | | |
| **Smoker,** n (%) | 20 (20.0) | 14 (18.2) | 6 (26.1) | 0.391 | | |
| **Underlying diseases** | | | | | | |
| **Diabetes,** n (%) | 19 (19.0) | 10 (13.0) | 9 (39.1) | <0.01 | | |
| **Malignant/Hematological neoplasia,** n (%) | 11 (11.0) | 5 (6.5) | 6 (26.1) | 0.017 | | |
| **Solid tumor,** n (%) | 6 (6.0) | 1 (1.3) | 5 (21.7) | <0.01 | | |
| **COPD,** n (%) | 10 (10.0) | 4 (5.2) | 6 (26.1) | <0.01 | | |
| **Cardiopathy,** n (%) | 22 (22.0) | 13 (16.9) | 9 (39.1) | 0.042 | | |
| **Neurologic disease,** n (%) | 6 (6.0) | 3 (3.9) | 3 (13.0) | 0.053 | | |
| **Hypertension,** n (%) | 31 (31.0) | 16 (20.8) | 15 (65.2) | <0.01 | 4.47 (1.36-14.66) | 0.013 |
| **Symptoms** | | | | | | |
| **Disnea,** n (%) | 23 (23.0) | 12 (15.6) | 11 (47.8) | <0.01 | | |
| Cough, n (%) | 53 (53.0) | 47 (61.0) | 6 (26.1) | <0.01 | | |
| Antibiotic treatment, n (%) | 60 (60.0) | 39 (50.6) | 21 (91.3) | <0.01 | | |
| Antiviral treatment, n (%) | 66 (66.0) | 48 (62.3) | 18 (78.3) | 0.212 | | |
| Lopinavir/ritonavir | 65 (65.0) | 47 (61.0) | 18 (78.3) | 1.0 | | |
| Hydroxycloroquine | 42 (42.0) | 33 (42.9) | 9 (39.1) | 0.250 | | |
| Interferon-beta | 27 (27.0) | 19 (24.7) | 8 (34.8) | 0.783 | | |
| Remdisivir | 7 (7.0) | 6 (7.8) | 1 (4.3) | 0.664 | | |
| Darunavir | 1 (1.0) | 1 (1.3) | 0 | 1.0 | | |
| Ritonavir | 1 (1.0) | 1 (1.3) | 0 | 1.0 | | |
| Oseltamivir | 2 (2.0) | 1 (1.3) | 1 (4.3) | 1.0 | | |
| **Tocilizumab,** n (%) | 11 (11.0) | 8 (10.4) | 3 (13.0) | 1.0 | | |
| **Oxygen saturation on admission,** median (IQR) | 94 (90-97) | 95 (93-97.2) | 90 (87-92) | <0.01 | | |
| **Lower oxygen saturation during the hospitalization,** median (IQR) | 92 (88-94) | 93 (90-95) | 83.5 (80.2-89) | <0.01 | | |
| **Bilateral pneumonia,** n (%) | 42 (42.0) | 23 (29.9) | 19 (82.6) | <0.01 | | |
| **Age-adjusted Charlson Index,** n (%) | 1.5 (0-5.7) | 0 (0-3) | 6 (5-8) | <0.01 | 1.55 (1.26-1.91) | <0.01 |
| **CALL Score,** median (IQR) | 10 (8-11) | 9 (7-11) | 11 (10-12) | <0.01 | | |
| **Length of hospitalization,** days, median (IQR) | 9.0 (7.0-15.2) | 9 (7-22) | 8 (5-14) | 0.109 | | |
| **Days at ICU,** median (IQR) | 11.0 (6.0-28.0) | 27 (8.7-28) | 9 (3-14.5) | 0.07 | | |
| **Days of hospital stay previous to ICU admission,** median (IQR) | 2 (0-3) | 2 (1.2-3.7) | 0 (0-2) | 0.05 | | |
| **Complications** | | | | | | |
| Cardiopathy | 18 (18.0) | 6 (7.8) | 12 (52.2) | <0.01 | | |
| ARDS | 30 (30.0) | 9 (11.7) | 21 (91.3) | <0.01 | | |
| Sepsis | 17 (17.0) | 8 (10.4) | 9 (39.1) | <0.01 | | |
| Kidney injury | 27 (27.0) | 12 (15.6) | 15 (65.2) | <0.01 | | |
| Liver injury | 25 (25.0) | 22 (28.6) | 3 (13.0) | 0.174 | | |
| Pulmonary embolism | 1 (1.0) | 0 | 1 (4.3) | 0.230 | | |

**COPD: chronic obstructive pulmonary disease, ARDS: acute respiratory distress syndrome**

**Table 3** **Summary of main laboratory results.**

| | Total (n=100) | Survivor (n=77) | Non-survivor (n=23) | p |
|---|---|---|---|---|
| **Lymphocyte count (10E3/µL),** median, IQR | 0.9 (0.7-1.3) | 1 (0.7-1.4) | 0.7 (0.5-1.1) | <0.01 |
| <1.3 | 55/77 (71.4%) | 36/55 (65.5) | 19/22 (86.4) | 0.094 |
| <0.8 | 31/77 (40.3%) | 18/55 (32.7) | 13/22 (59.1) | 0.042 |
| **Platelets (10E3/µL),** median, IQR | 155 (136-205.2) | 159 (136-239.5) | 155 (100-188) | 0.189 |
| <140 | 24/78 (30.8%) | 15/56 (26.8) | 9/22 (40.9) | 0.278 |
| ≥140 | 54/78 (69.2%) | 41/56 (73.2) | 13/22 (59.1) | |
| **C-reactive protein (mg/dL),** median, IQR | 4 (2-9.6) | 2.7 (1.5-6.5) | 6.3 (3.3-17.6) | <0.01 |
| **Procalcitonin (µg/L),** median, IQR | 0.05 (0.03-0.13) | 0.04 (0.03-0.08) | 0.12 (0.1-0.5) | <0.01 |
| <0.1 | 53/79 (67.1%) | 44/56 (78.6) | 9/23 (39.1) | <0.01 |
| ≥0.1 a <0.25 | 12/79 (15.2%) | 5/56 (8.9) | 7/23 (30.4) | 0.022 |
| ≥0.25 a <0.5 | 6/79 (7.6%) | 4/56 (7.1) | 2/23 (8.7) | 1.0 |
| ≥0.5 | 8/79 (10.1%) | 3/56 (5.4) | 5/23 (21.7) | 0.042 |
| **D-dimer (ng/mL),** median, IQR | 284 (219-794) | 274 (208-680.5) | 2010 (565-) | 0.154 |
| **ALT (U/L),** median, IQR | 24 (15-37) | 24.5 (15-38.7) | 24 (17-34) | 0.754 |
| ≤41 | 64/79 (81.0%) | 44/56 (78.6) | 20/23 (87.0) | 0.533 |
| >41 | 15/79 (19.0%) | 12/56 (21.4) | 3/23 (13.0) | |
| **LDH (U/L),** median, IQR | 256 (192.5-345.7) | 226 (191-297) | 316 (224-434) | 0.047 |
| ≤250 | 32/66 (48.5%) | 28/49 (57.1) | 4/17 (23.5) | 0.024 |
| 250-500 | 28/66 (42.4%) | 17/49 (34.7) | 11/17 (64.7) | 0.046 |
| >500 | 6/66 (9.1%) | 4/49 (8.2) | 2/17 (11.8) | 1.0 |
| **IL-6 (pg/mL),** median, IQR | 166.3 (61.4-) | 166.3 (61.4-) | - | - |
| **Blood urea nitrogen,** (mg/dL), median, IQR | 31 (19-79) | 21 (17-31) | 106 (61.7-205.7) | <0.01 |
| **Ferritin (µg/L),** median, IQR | 598 (267-1048.5) | 494 (153-681) | 2922 (676-) | 0.222 |
| **NTproBNP (ng/L),** median, IQR | 1036 (274-3981) | 465 (74-2500.5) | 1520.5 (588.2-5900) | 0.012 |

mum of 1 day and a maximum of 14 days. Forty-seven percent of the patients stated that they had had previous contact with a person diagnosed with COVID-19, either proven or probable.

$O_2$ saturation at the time of first examination ranged from a minimum of 80% to a maximum of 99%, with a median of 94% (IQR=90-97). A total of 19.8% of patients had saturation <90% on admission.

Sixty-three percent of the patients presented alterations in the chest X-Ray on admission, compatible with the diagnosis of pneumonia (Table 1). Radiological images were classified as bilateral pneumonia in 42% of patients and as unilateral in 21%. The infiltrates generally had a ground glass pattern but on some occasions they were clear alveolar infiltrates (Figure 3).

Overall, 70% of COVID-19 cases were admitted to hospital. The length of hospital stay for those patients who remained hospitalized ranged from a minimum of 1 day to a maximum of 32 days, with a median of 9 days (IQR=7.0-15.2). Thirteen patients required admission to the ICU during the course of their hospitalization, with a minimum of 2 days and a maximum of 28 days of stay and a median of 11 days (IQR=6.0-28.0). The mortality rate of these patients admitted to ICU was 38.5% (5/13). The median time from the onset of symptoms associated with COVID-19 in these patients until they were admitted to the ICU was 5 days (IQR=1.5-9.5) with a minimum of 1 day and a maximum of 13 days. Patients admitted to the ICU were previously hospitalized on the ward for a median of 2 days (IQR=0-3) with a minimum of 0 days and a maximum of 6 days.

Fourteen patients of our study cohort also showed other type of infections (n=17). Three of them were coinfections present at the same time as the diagnosis of SARS-CoV-2 and 14 were nosocomially acquired. The origin of all of them was

**Table 4** Comparative study in terms of severity scale (CALL score)

| | Class A and B (low and intermediate risk) n=29 | Class C (high risk) n=37 | p |
|---|---|---|---|
| **Age,** median, IQR | 51 (34.5-71) | 76 (64-86) | <0.01 |
| **Charlson Index,** median, IQR | 0 (0-5) | 4 (2-6.5) | <0.01 |
| **Oxygen saturation on admission,** median, IQR | 95 (94-97) | 92 (88-95) | <0.01 |
| **Dyspnoea,** n, % | 4/29 (13.8%) | 15/37 (40.5%) | 0.027 |
| **Antibiotic treatment,** n, % | 19/29 (65.5%) | 33/37 (89.2%) | 0.032 |
| **Complications** | | | |
| **Cardiopathy,** n, % | 2/29 (6.9%) | 3/37 (35.1%) | <0.01 |
| **ARDS,** n, % | 6/29 (20.7%) | 18/37 (48.6%) | 0.023 |
| **Kidney injury,** n, % | 5/29 (17.2%) | 28/37 (48.6%) | 0.01 |
| **Survivor at 30-day follow-up (at home),** n, % | 26/29 (89.7%) | 18/37 (48.6%) | <0.01 |
| **Laboratory** | | | |
| **Lymphocyte count,** median, IQR | 1.3 (1.1-1.5) | 0.7 (0.4-0.9) | <0.01 |
| **C-reactive protein,** median, IQR | 2.3 (1.3-4.7) | 5.3 (2.8-11.8) | <0.01 |
| **Procalcitonin,** median, IQR | 0.04 (0.03-0.06) | 0.09 (0.04-0.3) | <0.01 |
| **LDH,** median, IQR | 212 (190.5-267.5) | 283 (211.5-399.5) | <0.01 |

**ARDS: acute respiratory distress syndrome**

urinary (n=6), respiratory (n=5), bloodstream (n=4, 2 primary bacteremia and 2 catheter-related bacteremia), gastrointestinal (n=1) and catheter-related (n=1) infections. The most frequently isolated microorganisms were *Escherichia coli* (n=5), *Staphylococcus epidermidis* (n=2), *Staphylococcus aureus* (n=1), *Enterobacter cloacae* (n=1), *Klebsiella pneumoniae* (n=1), *Micrococcus luteus* (n=1), *Enterococcus faecalis* (n=1), *Staphylococcus haemolyticus* (n=1), *Aspergillus fumigatus complex* (n=1), Respiratory Syncytial Virus (n=1) and *Clostridium difficile* (n=1). Nine cases of proven bacterial sepsis were detected among 17 patients with sepsis syndrome.

Overall, 60.0% of patients received antibiotic treatment and 66.0% of patients received antiviral treatment, with lopinavir/ritonavir (65%) or hydroxychloroquine (42%) in an empirical basis. The main treatments are shown in Table 2. A greater use of antibiotics was observed in patients who died compared to survivors (91.3% vs 50.6%, p<0.01) but no significant differences were detected between both groups in terms of any type of antiviral or monoclonal antibody administered as treatment to the COVID-19.

Laboratory findings showed lymphopenia in 71% of patients diagnosed with COVID-19 with analytical determination on admission. Fourteen of the 23 patients with D-dimer determination (60.9%), had values greater than 250 ng/mL. IL-6 was only measured in 3 patients of our cohort but values were elevated in all the cases. Lymphocyte levels were lower in patients who died (p<0.01) compared to those who survived. C-reactive protein, procalcitonin, LDH, blood nitrogen-urea and NTproB-NP values were significantly higher in non-survivors compared to survivors at 30-60 days after diagnosis of COVID-19 (Table 3).

The median CALL score of the total patient cohort was 10, corresponding to Class C severity with a probability of more than 50% high risk of disease progression. The minimum CALL score was 4 (Class A) and the maximum was 13 (Class C) (Table 2). A significantly higher CALL score (p<0.01) was observed in patients who died compared to those who did not die (11 vs 9). When comparing patients with low-intermediate severity (Class A and B CALL score) with patients with high severity (Class C, CALL score), it was observed that those with greater probability of disease progression (Class C) presented greater age (p<0. 01), higher Charlson index (p<0.01), more dyspnea (40.5% vs 13.8%, p<0.01), higher percentage of antibiotic use (89.2% vs 65.5%, p<0.05) and a greater presence of complications such as heart disease (p<0.04), respiratory distress (p<0.05) and kidney damage (p=0.01) (Table 4). The percentage of survivors was lower in this group (48.6% goes 89.7%, p<0.01). Regarding laboratory findings, lymphocyte, C-reactive protein, procalcitonin and LDH levels were significantly higher in these high severity patients (p<0.01).

At 30 days of follow-up after positive PCR test for SARS-CoV-2, 23 patients (23%) had died, 72 (72%) were recovering

at home, 2 (2%) remained hospitalized and 3 (3%) were in the ICU. After 60 days of follow-up, no more deaths were detected in our cohort, one of the 2 patients who had been hospitalized at 30 days remained hospitalized and the other was at home. As for the ICU patients, 2 remained hospitalized at 60 days and the third was discharged after 49 days of admission. Figure 2 shows the distribution of patients who survived and died by age groups (decades).

A comparative study between live and dead patients 30-60 days after diagnosis of COVID-19 showed that dead patients were significantly older ($p<0.01$), had a higher Charlson index ($p<0.01$) and had a higher percentage of bilateral pneumonias ($p<0.01$). The frequency of complications was higher in non-survivors than in survivors. Table 2 shows this comparison and the profile of the deceased patients in detail. By performing a multivariate analysis including variables with statistical significance in the univariate analysis less than 0.01, the presence of hypertension and age-adjusted Charlson Index were identified as risk factors associated with death.

The age of the deceased patients ranged from 39 to 99 years with a median of 85 years (IQR=79-93). Only 3 of the 23 deceased patients (13%) were under 75 years of age. One of them (51 years old) had diabetes mellitus, Cushing's disease, high blood pressure, hepatitis C and SARS-CoV-2 coinfection with RSV. Another (45 years old) had diabetes mellitus, high blood pressure, morbid obesity, chronic renal disease, *Clostridium difficile* colitis and was a carrier of a biological mitral prosthesis. The third, was a 39 years old patient with epidermoid carcinoma of the cervix treated with surgery in 2014 and currently with stage IV anal canal carcinoma in progression, with peritoneal carcinomatosis in treatment with palliative chemotherapy. The 23 patients who died had a median Charlson Index of 6 (IQR=5-8). Eleven patients (47.8%) had a BMI greater than 30 and 3 were immunosuppressed. Nineteen patients (82.6%) had bilateral pneumonia and 4 (17.4%) had unilateral pneumonia.

## DISCUSSION

Our study shows a high mortality of the first hundred patients treated with COVID-19 in our institution, associated with advanced age and the presence of serious underlying diseases in our population. Twenty of the 23 (23%) deceased patients were over 75 years of age and all had serious comorbidities.

The mortality in our series is similar to that reflected by Western countries such as Italy, UK, USA and others (19% to 39%) [3, 13-15] and differs significantly from that reported from China or Korea (0.9% to 7.5%) [4, 16-20]. It is clear that when calculating mortality the denominators matter [17, 21, 22].

The basic reason for these differences are to be found in the median age of the respective populations which was between 62 and 65.5 years in Western publications [3, 13, 15] and between 41 and 47 in the case of Chinese publications [4, 18]. In addition, comorbidity appears as a clear factor of poor prognosis as well as the level of care [23, 24].

Mortality in the case of China is even more surprising, since the initially reported cases considered pneumonia as a constant in clinical presentation [2, 25-28], to the extent that the presence of certain lesions in the thoracic CT was considered a diagnostic criterion in the early stages [29-31]. However, as demonstrated by our first 100 microbiologically confirmed patients, pneumonia was absent in a high proportion of cases and is even less frequent in subsequent series where diagnostic suspicion is spread to less severe or asymptomatic patients [4, 19, 32].

An interesting aspect of our series is the evaluation of the ability to predict and anticipate patients with poor clinical evolution. Our study has used the CALL score [11] and validated its usefulness. For example, all the patients sent home, evolved well during the follow-up and did not require admission in the two months of follow-up.

No antiviral treatment has been shown to be effective to date. Most patients in our cohort were treated with lopinavir/ritonavir but none of the different types of antivirals administered during this first period have shown significant differences between patients who survived and those who died [33-39].

Our results and previous studies show that lymphopenia is common in COVID-19 cases, suggesting that SARS-CoV-2 infection causes an inhibition of the cellular immune response and a significant number of complications as seen in our patient cohort. We have also observed that elevation of markers such as C-reactive protein and procalcitonin is common in severe COVID-19 cases [4, 40].

Our study aims to contribute to a better understanding of the clinical evolution and mortality among the cases of COVID-19 in different continents, with a follow-up perspective of more than two months. The real mortality will not be known until the true dimension of the epidemic can be analyzed through population studies and the number of deceased cases can be related to the underlying diseases and the situation of the hospitals at different times of the epidemic.

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## CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest

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