COVID-19 - Health care management

First wave of the COVID-19 pandemic in Madrid: handling the unexpected in a tertiary hospital

LUCÍA HERNÁNDEZ-RIVAS, EVA FERNÁNDEZ-BRETON, TERESA PEDRAZ, CLAUDIA GARCÍA-VAZ, JOSÉ MIGUEL CANTERO-ESCRIBANO, MERCEDES MARTÍNEZ-CASTRO, VERÓNICA PÉREZ-BLANCO, ANA ROBUSTILLORODELA
Department of Preventive Medicine, La Paz University Hospital, Madrid, Spain

Keywords

COVID-19 • SARS-CoV-2 • Pandemic • Epidemic curve

Summary

Introduction. *The COVID-19 pandemic was declared on March 11th, 2020. By the end of January, the first imported cases were detected in Spain and, by March, the number of cases was growing exponentially, causing the implementation of a national lockdown. Madrid has been one of the most affected regions in terms of both cases and deaths. The aim of this study is to describe the epidemic curve and the epidemiological features and outcomes of COVID-19 patients hospitalized in La Paz University Hospital, a tertiary hospital located in Madrid.*
Methods. *We included confirmed and probable COVID-19 cases admitted to our centre from February 26th to June 1st, 2020. We studied trends in hospitalization and ICU admissions using joinpoint regression analysis.*
Results. *A sample of 2970 patients was obtained. Median age was 70 years old (IQR 55-82) and 54.8% of them were male. ICU admission rate was 8.7% with a mortality rate of 45.7%. Global CFR was 21.8%. Median time from symptom onset to death was 14 days (IQR 9-22).*
Conclusions. *We detected an admissions peak on March 21st followed by a descending trend, matching national and regional data. Age and sex distribution were comparable to further series nationally and in western countries.*

Introduction

Since a cluster of patients with pneumonia of unknown origin was detected in Wuhan, China [1], SARS-CoV-2 infections [2] have rapidly spiked around the world, with COVID-19 being declared a pandemic by WHO on March 11th 2020 [3].
On January 31st 2020, the first imported cases were detected in Spain and by February 28th, patients with no epidemic link started to be diagnosed. By March 13th, cases had been confirmed in all 50 provinces in the country and started to grow exponentially. Some non-pharmacological public health measures were implemented in order to control the epidemic, the most important being a national lockdown on March 14th. On March 26th, at the peak of the epidemic in Spain, 9181 cases were reported on a single day and up to 900 deaths were reported in one day. From April 28th on, as cases had been consistently decreasing, the country gradually started to reopen, and the state of alarm ended on June 21st.
In late February, the first series of patients with COVID-19 infection in China were published [4-6], with patients being predominantly adult males, and case fatality rates (CFR) ranging from 1.4 to 28.3% [4]. Following series in other countries present some variability in age and sex distribution and CFR, which can be explained by differences in the base populations, the burden of the epidemic and overload in healthcare facilities [7, 8].
The Community of Madrid was one of the most affected regions in Spain. It has registered the highest number of cases and deaths in the country. Healthcare facilities were overwhelmed and close to saturation, with limited capacity for testing all of the suspected cases during the peak of the epidemic. Surveillance systems were also challenged by the rapid surge in cases, with no capacity for contact tracing in mild cases.
La Paz University Hospital is a tertiary care public hospital located in Madrid, with 1300 beds and a catchment area with a population of more than 500000. In 2018, 48945 patients had been hospitalized in this centre.
The aim of this study is to describe the epidemic curve of hospitalization and the epidemiological features and outcomes of all of the patients admitted in our centre with confirmed or highly suspected infection by SARS-CoV-2 until June 1st 2020.

Methods

Study Population

The current study included all individuals who were admitted to La Paz University Hospital from February 26th to June 1st 2020.
COVID-19 diagnosis included confirmed cases (any individual with positive reverse transcriptase

polymerase chain reaction (RT-PCR) assay) and probable cases (any individual meeting clinical criteria with an epidemiological link or radiological evidence compatible with SARS-CoV-2 infection) [9].

Data Collection

Data collection effort was conducted by the department of Preventive Medicine in La Paz University Hospital as a part of their regular activities. We registered every new patient admitted to the hospital daily on a database. The epidemiological data and outcomes (discharge, transfer or death) were obtained from electronic medical records, including clinical notes for date of symptoms onset (DXC-HCIS - Healthcare Information System). Country of origin was grouped following WHO regions. Intensive care unit (ICU) admissions were also recorded.

Ethical considerations

This study was conducted in accordance with the tenets of the Declaration of Helsinki and was reviewed and approved by the Research Ethics Committee of La Paz University Hospital (PI-4195).

Statistical Analysis

All statistical analysis was performed using R. Continuous variables were presented as means and standard deviations (SD) or medians and interquartile ranges (IQR), as appropriate. Categorical variables were summarized in terms of frequency (percentage).
Means for continuous variables were compared by independent group t-test when the data were normally distributed. The Mann-Whitney test was used when the data were non-normally distributed. Proportions in categorical variables were compared using the χ^2 test, although Fisher´s exact test was used in cases where data was limited.
Temporal trends in hospitalization and ICU admissions were evaluated using joinpoint regression analysis. This method describes changes in data trends by connecting different line segments by "joinpoints", or points where the trend significantly changes (increases or decreases). Those points are presented with a 95% confidence interval (95% CI). We also present daily percent changes (DPC) of the different trends identified. As all lines are based on the log-linear model, the joinpoint regression model is free from complex spline selections and sensitivity concerns [10]. Joinpoint analyses were performed using the Joinpoint software from the US National Cancer Institute [11].

Results

A total of 3007 COVID-19 patients were hospitalized in La Paz University Hospital before June 1st, 2020. After excluding 37 patients that were still hospitalized as of June 1st, the final analysis included 2970 individuals. Of these, 2627 were confirmed cases diagnosed by SARS-CoV-2 RNA detection while 343 were probable cases, diagnosed by clinical or radiological criteria.
Median age was 70 years (IQR 55-82) ranging from 0 to 102 years. Of all patients, 54.8% were male, while 45.2% were female. Median age in females was 71 years (IQR 55-83) while in men was 69 years (IQR 56-80), p-value = 0.01.
CFR was 21.8% and ICU admission rate was 8.7%. The ICU mortality rate was 45.7%. Patients' characteristics, sex differences and outcomes are presented in Table I.
Median age in patients with Europe as their WHO Region of birth was 74 years (IQR 61-84), whilst, in those from the Americas region, it was 52 years (IQR 40-60). ICU admission rate was 7.8% for the Europe region and 12.1% for the Americas region. Mortality rate for the Americas region was 8.1% while for the Europe region it was 24.8%.
Most patients hospitalized were males above 50 years of age. For patients admitted in the ICU, most of them were males aged between 60 and 70 years old. Age and sex distribution, and hospitalisation status are shown in Figure 1.

Tab. I. Patients' characteristics and outcomes.

	Global	Female	Male	p-value
Age *median years (IQR)*	70 (55-82)	71 (55-83)	69 (56-80)	0.01
Hospitalization				
Patients admitted	2970	1342 (45.2%)	1628 (54.8%)	
Patients who died	646 (21.8%)	232 (17.3%)	414 (25.4%)	< 0.01
ICU				
Patients admitted	258 (8.7%)	78 (5.8%)	180 (11.1%)	< 0.01
Patients who died	118 (45.7%)	29 (37.2%)	89 (49.4%)	0.06
WHO Region of birth				
Europe	2406 (81.0%)			
Americas	480 (16.2%)			
Eastern Mediterranean	25 (0.8%)			
Africa	5 (0.2%)			
South-Eastern Asia	7 (0.2%)			
Western Pacific	46 (1.6%)			

Fig. 1. COVID-19 hospitalized population pyramid. Age and gender distribution of hospitalizations are shown here. Hospitalization status is added in terms of ICU admissions and deaths, showing its age and gender distribution

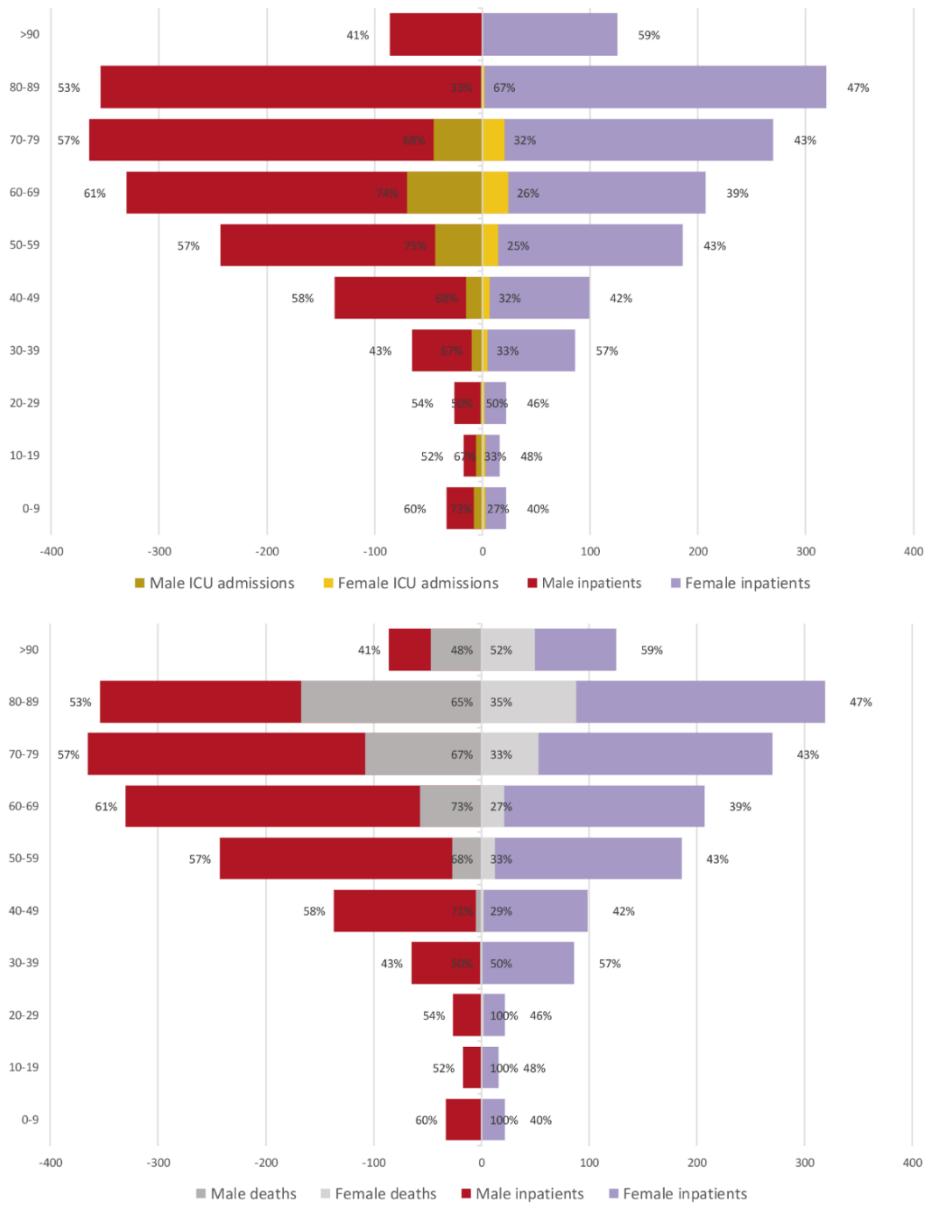


Figure 2 shows length of stay in days of hospitalization. Figure 3 shows time from symptom onset to hospital admission. Median length of hospital stay for all patients was 8 days (IQR 4-15). For critically ill patients, median length of hospital stay was 25 days (IQR 13-40). For patients who died during hospitalization, median length of hospital stay was 7 days (IQR 4-15).

Two comparisons were made regarding length of hospital stay: among patients who died and survivors, and among those who were admitted to ICU and those who weren't. Patients who died had shorter hospital stay. Patients admitted to ICU stayed longer. Differences were statistically significant.

Comparisons were made among patients who died and survivors and among those who were admitted to ICU and those who weren't. Patients who died had less time from symptom onset to hospital admission. No significant differences were found regarding ICU admission status.

Median time from symptom onset to hospital admission was 7 days (IQR 5-10), being 7 days (IQR 5-10) for patients admitted in ICU and 6 days (IQR 3-9) for patients who ended up dying.

For patients admitted to the ICU, median stay in days of ICU was 12 (IQR 4-24), with a minimum of 0 days (less than 24 hours) and a maximum of 83. Median time, in days, from symptom onset to admission to the ICU was 10 (IQR 7-13).

Median time, in days, from symptom onset to death was 14 (IQR 9-22), with a minimum of 3 days and a

Fig. 2. Length of stay in days of hospitalization. Boxplot distribution is shown here.

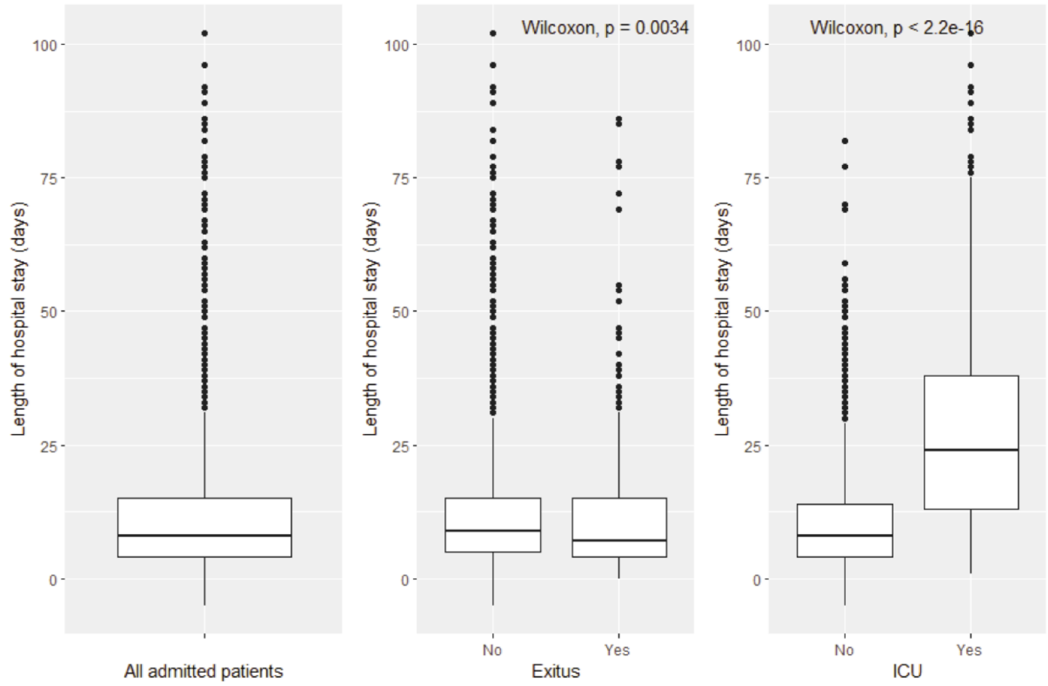
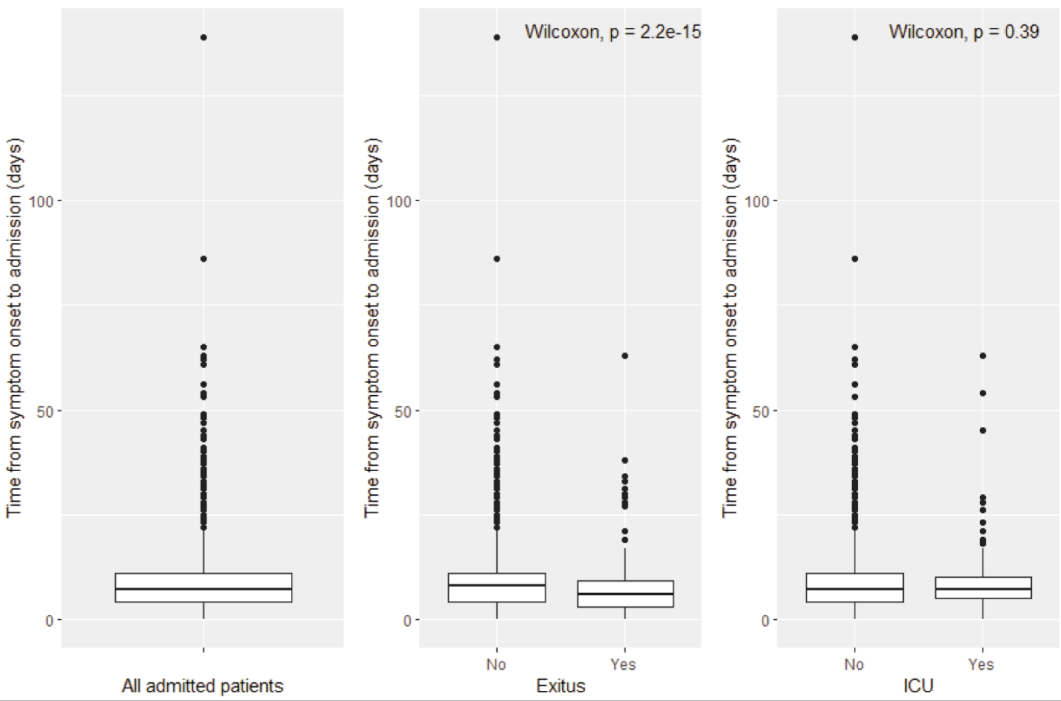


Fig. 3. Time from symptom onset to hospital admission. Boxplot distribution is shown.



maximum of 100 days. For patients who died in the ICU, median time from symptom onset to death was 29 days (IQR 18-39).

Trends of admissions

The epidemic curve according to symptom onset date and date of diagnosis is shown in Figure 4.

On March 9th, (95% IC 6-17) a significant change in the trend of admitted patients was identified, and the joinpoint analysis revealed a significant decrease in the daily percent change (DPC) of admitted patients after that date (46.7% on the first segment versus 9.9% on the second one). An additional joinpoint was identified on March 21st (95% IC 19-28), signalling a change in

Fig. 4. Number of COVID-19 cases by date of diagnosis and date of symptom onset.

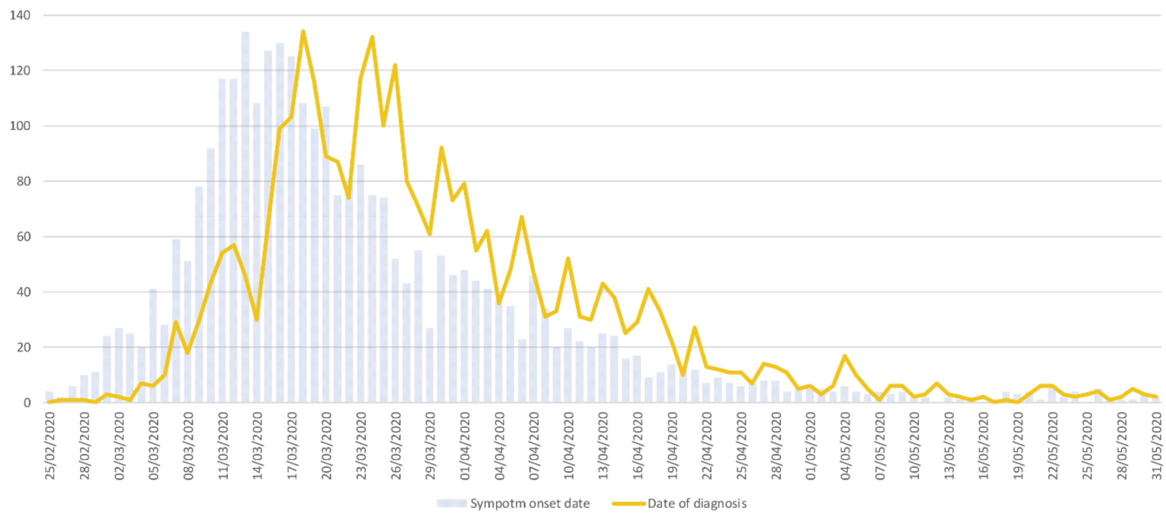


Fig. 5. Joinpoint regression model: admitted patients by date of diagnosis.

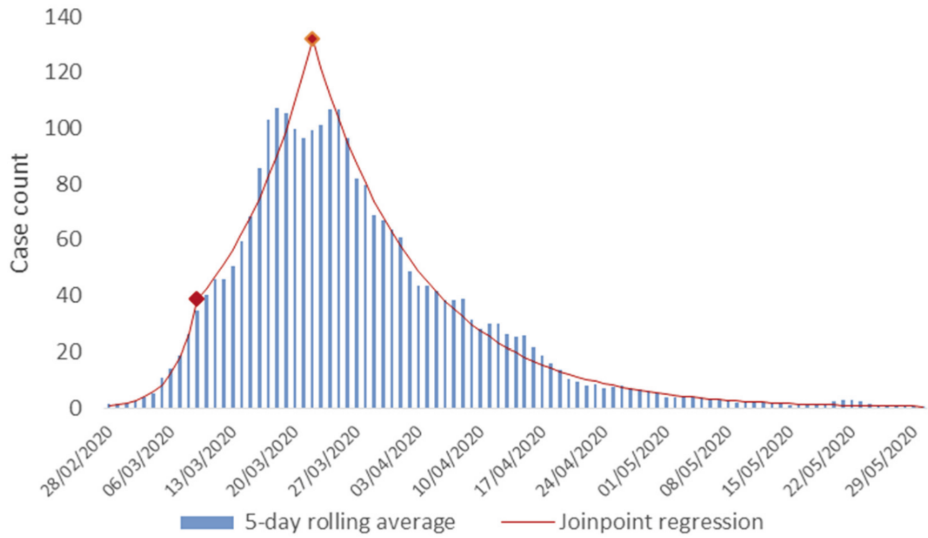
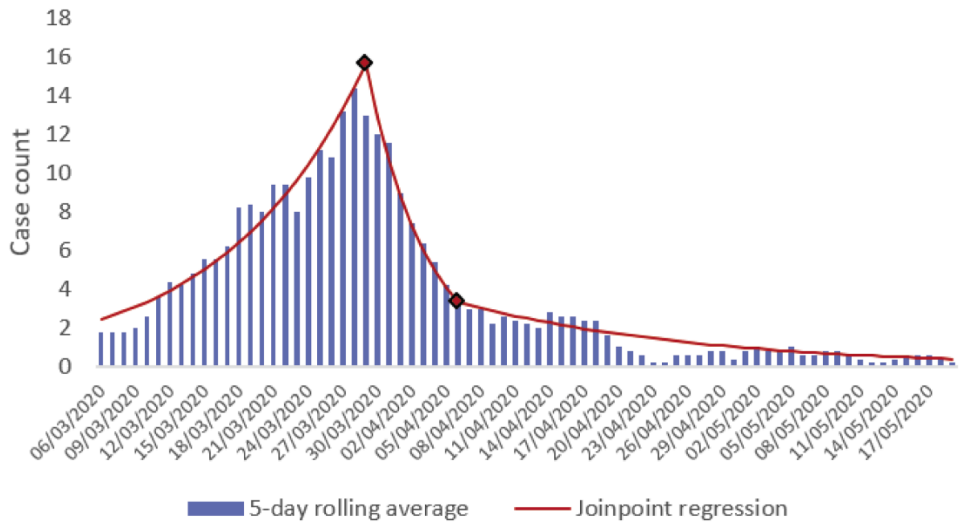


Fig. 6. Joinpoint regression model: ICU admissions.



trend, with the number of admitted patients starting to decrease and the DPC going from the previous 9.9 to -7.9%.

Trends of ICU admissions

On March 22nd, (95% IC March 21st-25th) a significant trend change was detected in ICU admissions, going from a positive DPC to a negative one (8.4 vs -17.5%). On March 31st (95% IC March 29th-April 2nd) another joinpoint indicates a new change in trend, in this case not changing the direction, but slowing down the DPC from -17.5 to -4.8.

Discussion

The first confirmed COVID-19 case was admitted to our centre on February 25th, 2020. The present study describes a series of patients who were hospitalized with a COVID-19 diagnosis between that date and June 1st in La Paz University Hospital and trends of admissions over that period.

The evolution of the COVID-19 pandemic observed in our hospital was very similar to the epidemic curve observed in Spain and the whole Community of Madrid region. After some cases in February, an exponential growth was observed during the first weeks of March. Measures in response to the pandemic were taken nationally on March 14th under the state of alarm decree [12] and the epidemic curve reached its peak two weeks later, around March 26th, with 3383 new hospitalizations in the Community of Madrid region [13, 14].

In our study, a joinpoint regression detected a peak of COVID-19 hospital admissions on March 21th (95% IC 19-28) followed by a decrease, matching the observed regional and national data. The change in trend found on March 9th (95% IC 6-17) was not present in the epidemic curve of the Community of Madrid region or Spain. However, this change could be explained by the epidemic control measures adopted in Madrid on March 10th, which could have predisposed Madrid residents to move to second residencies in other regions, thus affecting the expected number of cases and hospitalizations [15].

Another aspect that affects the epidemic curve observed in our centre is hospital bed occupancy. Due to the exponential growth in cases, the hospital experienced progressive shortage of hospital beds, which influenced the number of new patients susceptible of admission.

To cope with the major pressure the pandemic put on the healthcare system, our hospital had to quickly increase the number of hospitalization and ICU beds.

Wards were organized as COVID-19 cohorts or "no COVID-19" wards. At the beginning of the pandemic there were only a few COVID-19 cohorts but, due to community transmission and the consequently rapid increase of cases, by mid-March almost every ward in the hospital was turned into a cohort. A few wards remained "no COVID-19", destined to care for vulnerable patients whose assistance could not be delayed (Haematology, Oncology, Nephrology, Stroke Unit, Coronary Unit and Emergency surgeries). To take care of critical patients, operating rooms and post-anaesthesia care units were adapted into ICU, making it possible to increase the ratio of ICU beds by 500%.

The age and sex distribution of our cohort is comparable to further series from Spain and other western countries [7,18,19]. Patients included in the first cohorts from China were younger (median age of 47 years in Guan et al. [4] and 56 in Zhou et al. series [20]), reflecting main differences in the demographic structure of the populations.

The proportion of patients admitted to an ICU was 8.7% and for most age groups, the proportion of males hospitalized and admitted to the ICU was significantly higher than females. A study in a secondary hospital in Madrid reported a lower figure (6.7%) despite having a similar distribution of sex and patients being younger [16]. This could be attributed to a difference in admission criteria in each hospital's ICU, as well as their capacity. Our centre, being a reference hospital, also received ICU patients transferred from other hospitals of the region.

CFR varies according to admission criteria (stricter admission criteria lead to higher CFR) and the distribution of sociodemographic variables in the population. It is also affected by the burden on the healthcare system, so two hospitals in a different region of the same country can show dramatic differences in the CFR, as shown in China when comparing Hubei with other regions [20]. Mortality in our cohort is similar to that observed in New York, another hotspot for COVID-19, [19] and lower than the UK multicentre cohort, which reported a 33% mortality [18]. However, it is much higher than the figure reported in Italy (7.2%), [7] likely because the work includes data from the whole country and not only the most affected regions (Lombardy and Veneto).

In our study, 16.2% of all patients were born in a country from the Americas WHO Region of birth. Approximately, 9.3% of the Community of Madrid population were born in America [21]. Most of these patients were from South and Central America and the Caribbean, only two patients of this region were North Americans. Our data showed that these patients were younger than European patients, with a difference of 20 years in median age, and had a higher ICU admission rate (12.1%), although their mortality rate was lower (8.1%). 97.8% of the Europe WHO Region of birth patients were Spanish. These findings are similar to those reported in other studies of the region [16].

Differences in age can be explained by the demographics of the Hispanic population in our country. Younger patients tend to have less comorbidities, thus having more chances to be admitted to an ICU and having a better prognosis. A systematic review and meta-analysis by Shirley Sze et al. which explored the relationship between ethnicity and clinical outcomes in COVID-19 did not find differences between Hispanic and non-Hispanic patients [22].

Despite all, our work has some limitations. First, the study included patients diagnosed by PCR (confirmed cases) and patients diagnosed using clinical and epidemiological or radiological criteria (probable cases). Furthermore, case definition criteria changed during this period, only introducing probable case definition by the end of March 2020. Due to all of this, we cannot exclude heterogeneity among cases. Another potential bias is that we only included hospitalized patients, therefore we lack information about mild cases, which are more likely handled in Primary Health Care. In addition, due to the overload of Madrid Healthcare System, paediatric and maternal urgent care was redistributed, and our hospital was one of the few attending these patients. Because of this, our results cannot be widely generalized.

Nevertheless, the fact that our study was conducted in a tertiary hospital, including all admitted COVID-19 cases during Spain's first outbreak is proof of the relevance of this work. This allows for a big sample size which, despite the limitations, we believe is representative of the COVID-19 hospitalized Madrid population.

The use of joinpoint regression is another highlight from our study. Joinpoint regression models are useful tools to evaluate efficiently time-trend curves and to identify a phase change in the pandemic [23].

Conclusions

In summary, our hospital had to cope with a great number of COVID-19 patients and the exponential growth of admissions from the end of February until approximately a week after national lockdown (March 21st), when a peak in hospitalizations was detected. As reported in other studies, most affected patients were males over 50 years old. This group had both higher ICU admission and mortality rates.

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Conflict of interest

All authors report no conflicts of interest relevant to this article.

Authors' contributions

LHR, EFB, TP, CGV, MCM and JMCE equally contributed to data collection, design of the study, performed the analysis, interpretation of results and drafting of the article.

VPB and ARR contributed to data collection, design of the study, interpretation of results, drafting of the article and revised the article critically.

Ethics approval and consent to participate

The study was approved by an ethical committee. This manuscript has been read and approved by all authors and has not been published and is not under consideration for publication elsewhere.

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Correspondence: Lucía Hernández-Rivas, Department of Preventive Medicine, La Paz University Hospital, Madrid, Spain. E-mail: lhrivas@salud.madrid.org

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