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## Health Indicators in Hospitalized Patients With SARS-CoV-2 Pneumonia: A Comparison Between the First and Second Wave



### Indicadores sanitarios en pacientes hospitalizados por neumonía SARS-COV-2: comparación entre la primera y segunda ola

Dear Editor,

The first cases of coronavirus disease 2019 (COVID-19) were identified in Wuhan, China<sup>1</sup> a year ago. However, few studies have been published comparing the characteristics and clinical outcomes of hospitalized patients with pneumonia secondary to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) of the first and second wave of the pandemic in Europe. Moreover, it has not been investigated whether patient management and health indicators improved during the second wave as a result of the experience acquired during the first. The objective of this study is to compare the characteristics and outcomes of hospitalized patients with COVID-19 of the first and second wave of the pandemic.

Data were collected from the medical reports of patients diagnosed with Covid-19 and admitted to our hospital, from February 2020 (date of first Covid-19 diagnosis) to December 31 (first wave until June 30; second wave since July 1). The study was approved by the Institutional Review Board (#2020/194). A case of Covid-19 was confirmed in the presence of a positive result in the reverse transcription polymerase chain reaction test on samples obtained from nasal or throat swabs, or a positive antigen test performed in accordance with the Spanish Ministry of Health recommendations.<sup>2</sup> Only laboratory-confirmed cases were considered for analysis. All patients diagnosed with Covid-19 pneumonia<sup>3</sup> were hospitalized and included in the study. All data were recorded at admission (+1 day). Patient were eligible for intensive care unit (ICU) admission if required mechanical ventilation or had a fraction of inspired oxygen (FiO<sub>2</sub>) of at least 60% or more. Radiological anomalies were collected from reports of the Unit of Radiology.

We assumed missing data occurred at random depending on the clinical variables and performed multiple imputations using chained equations. Missing values were predicted from other outcome predictors. We created 100 datasets with identical known information but with differences in imputed values reflecting the uncertainty associated with imputations. In total <1% clinical data items were imputed (see Table 1). We used Chi-square test to compare proportions and Mann-Whitney *U* test for comparison of quantitative variables. Logistic regression analyses were performed to investigate the effects of the two waves on outcomes (risk of death, ICU admission and the risk for mechanical ventilation). For this purpose, regression models were tested using non-parametric techniques, adjusted for the predictors of the DALSH score (diabetes, age, lymphocytes, oxygen saturation, pH).<sup>4</sup> Results are presented as Odds Ratio (OR) with 95% confidence intervals (95%CI). Statistical analyses were carried out in R using the mice and mgcv packages. These packages are freely available at <http://cran.r-project.org>.

Fig. 1 shows the number of hospitalized patients by month during the two waves. Table 1 shows the characteristics of patients

at baseline. As compared to the first wave, during the second wave, patients were significantly older, had fever less frequently, received the same medications and had similar comorbidities as patients of the first wave. Of note, the prevalence of heart failure was higher. Laboratory data show a lower inflammatory component (lower levels of lactate dehydrogenase and interleukin-6 and similar C-reactive protein levels) and lower concentrations of lymphocyte and platelets. In addition, respiratory distress (lower SaO<sub>2</sub>, PaO<sub>2</sub>/FiO<sub>2</sub> and SaO<sub>2</sub>/FiO<sub>2</sub> ratios) and bilateral consolidations on chest X-ray were more frequent in the second wave, whereas interstitial abnormalities were less frequent. A higher use of corticosteroids and remdesivir was observed in the second wave, whereas hydroxychloroquine was hardly administered (5%) and Lopinavir/ritonavir were no longer used.

The median length of hospital stay was significantly higher during the first wave [10 (7, 19) vs 9 (6, 13) days; *P* < .001]. Health indicators were poorer in the first than in the second wave (admission to ICU, 13% vs 11%; mechanical ventilation, 11% vs 7%; deaths, 17% vs 15%).

After adjusting for diabetes, age, lymphocyte count, oxygen saturation and pH (DALSH score), the risk for mechanical ventilation (OR 0.45, 95%CI 0.26–0.79) and for death (OR 0.52, 95%CI 0.31–0.85) were significantly lower in the second wave than in the first wave. The risk of admission to ICU (0.65, 95%CI 0.40–1.05) was also lower but without reaching significantly statistical association.

According to the results obtained, the length of hospital stay, use of mechanical ventilation and mortality were lower in hospitalized patients with COVID-19 pneumonia during the second wave, as compared to the first. All despite the fact that patients in the second wave were older and their characteristics were associated with a higher risk for developing severe COVID-19 (lower SaO<sub>2</sub>, PaO<sub>2</sub>/FiO<sub>2</sub> and SaO<sub>2</sub>/FiO<sub>2</sub> ratios).<sup>5</sup> These results persisted after adjustment for variables of severity (DALSH score).<sup>4</sup>

Previous studies with a different design also show that mortality decreased over time.<sup>6,7</sup> This cannot be attributed to demographic changes or variations in disease severity at presentation. Thus, whereas COVID-19 was approached as other severe respiratory diseases during the first wave, during the second wave the disease was managed based on the clinical experience acquired. As a result,

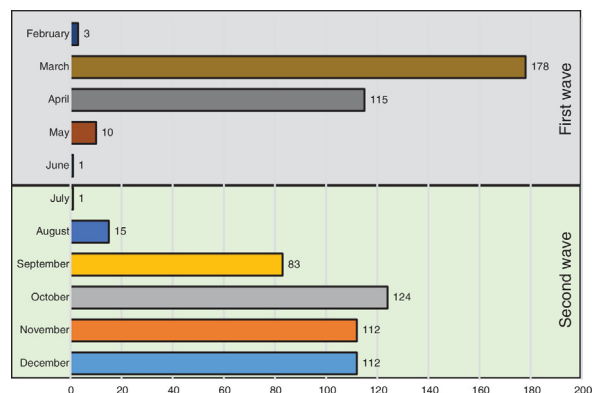


Fig. 1. Number of hospitalized patients by month during the two waves.

**Table 1**  
Clinical Characteristics of the Study Patients.

Characteristics	All Patients		Waves		P Value
	Missing	(n = 754)	First (n = 308)	Second (n = 446)	
Age, yr	0	69(58,80)	68(58,77)	71(58,82)	.032
Male sex	0	57%	59%	56%	.389
Temperature $\geq 37.5^\circ\text{C}$	1	28%	32%	28%	.031
Systolic blood pressure, mmHg	2	130(116,144)	130(119,142)	130(114,145)	.966
Diastolic blood pressure, mmHg	2	75(68,82)	74(67,81)	75(69,84)	.007
Heart rate, beats/min	7	82(74,92)	81(73,90)	82(74,92)	.395
<b>Symptoms</b>					
Fever	1	65%	75%	59%	<.001
Cough	1	71%	71%	71%	.963
Shortness of breath	1	55%	52%	57%	.119
Thoracic pain	3	8%	9%	8%	.593
Diarrhea	4	21%	23%	19%	.200
Anosmia	15	10%	8%	12%	.077
Dysgeusia	15	13%	11%	15%	.094
Confusion	3	4%	4%	4%	.707
<b>Treatment</b>					
ACEI	1	11%	11%	11%	.992
ARAI	2	26%	26%	27%	.912
Statins	1	39%	39%	40%	.704
Corticosteroids	1	6%	7%	5%	.247
Immunosuppressors	1	4%	5%	3%	.055
Anticoagulants	3	12%	10%	14%	.094
Antiplatelet agents	8	13%	12%	14%	.509
<b>Medical history</b>					
COPD	0	7%	8%	7%	.577
Arterial hypertension	0	51%	49%	53%	.248
Diabetes mellitus	0	24%	23%	25%	.665
Chronic renal disease	0	10%	9%	11%	.347
Coronary heart disease	0	9%	9%	10%	.684
Heart failure	2	10%	7%	12%	.035
Cancer	1	8%	7%	9%	.343
Systemic disease	2	7%	8%	7%	.589
Pulmonary disease	1	15%	15%	15%	.974
<b>Laboratory</b>					
White-cell count, $10^3$ cells/mm <sup>3</sup>	6	5.8(4.3,7.9)	5.7(4.3,7.4)	6.0(4.3,8.2)	.089
Lymphocyte count, $10^2$ cells/mm <sup>3</sup>	7	8.9(6.0,12.3)	9.7(6.4,14.0)	8.4(5.9,11.6)	<.001
Neutrophil count, $10^3$ cells/mm <sup>3</sup>	7	4.2(4.0,6.0)	3.9(2.8,5.6)	4.4(3.1,6.3)	.004
Platelet count, $10^3$ cells/mm <sup>3</sup>	6	188(143,256)	206(153,278)	177(138,235)	<.001
Haemoglobin, g/dL	9	13.5(12.1,14.7)	13.0(11.8,14.0)	13.8(12.5,14.9)	<.001
C-reactive protein, mg/dL	16	6.7(2.9,12.3)	6.6(2.9,12.8)	6.8(3.0,12.0)	.852
Lactate dehydrogenase, U/L	42	388(276,530)	439(320,587)	346(261,517)	<.001
Creatine kinase, U/L	47	80(49,143)	71(44,131)	85(52,155)	.006
Creatinine, mg/dL	10	0.9(0.7,1.2)	0.9(0.7,1.1)	0.9(0.8,1.2)	.005
Urea, mg/dL	8	41(31,60)	40(30,59)	41(31,61)	.618
D-dimer, ng/mL	24	754(448,1265)	707(422,1171)	807(477,1310)	.048
Interleukin-6, pg/mL	121	19(8,43)	28(12,54)	16(7,36)	<.001
<b>Gasometry</b>					
pH	73	7.45(7.43,7.48)	7.46(7.43,7.48)	7.45(7.42,7.48)	.028
PaCO <sub>2</sub> , mm Hg	74	33(30,37)	33(30,36)	33(30,37)	.108
PaO <sub>2</sub> , mm Hg	75	65(58,74)	67(59,76)	64(57,73)	<.001
HCO <sub>3</sub> <sup>-</sup> , mmol/L	76	23(21,25)	23(21,25)	23(21,25)	.677
SaO <sub>2</sub> , %	52	93(91,95)	94(92,95)	93(91,95)	.007
PaO <sub>2</sub> /FiO <sub>2</sub> ratio, mm Hg	75	309(276,353)	319(283,362)	303(272,346)	<.001
SaO <sub>2</sub> /FiO <sub>2</sub> ratio	52	443(433,452)	447(436,453)	443(431,452)	.007
<b>Radiologic</b>					
Unilateral consolidation	0	41%	42%	40%	.039
Bilateral consolidation		46%	38%	52%	
Interstitial abnormalities		7%	11%	5%	
Consolidation + interstitial		6%	9%	3%	
<b>Covid treatments</b>					
Hydroxychloroquine	0	37%	91%	5%	<.001
Antibiotics	0	93%	93%	93%	.824
Lopinavir/ritonavir	0	32%	77%	0%	<.001
Costicosteroids	0	67%	37%	87%	<.001
Tocilizumab	0	7%	10%	6%	.022
Remdesivir	0	7%	1%	11%	.001

ACEI, angiotensin-converting enzyme inhibitors; ARAII, angiotensin II receptor antagonists; COPD, chronic obstructive pulmonary disease. Data are percentages or medians (percentil25, percentil75).

clinicians started to use new drugs, prevalingly remdesivir and corticosteroids. Remdesivir had demonstrated its effectiveness in reducing time to recovery in hospitalized adults with Covid-19 and improving lower respiratory tract infection, although survival did not seem to improve with this drug.<sup>8</sup> Corticosteroids proved a benefit on survival in patients with respiratory insufficiency<sup>9</sup> and their use increased in the second wave. New practices (prone position)<sup>10</sup> were also incorporated in the second wave. In addition, during the first wave it was observed that clinical outcomes improved with the use of assisted ventilation or high-flow nasal cannula at the early stages of the disease, so they were more frequently used during the second wave.

The strengths of the study lie in that it is the only hospital of the Health District (450,000 population) where COVID-19 patients are hospitalized, and all associated clinical data are available on electronic medical records. The major limitation of this study is that it only includes patients from a single healthcare area.

Although COVID-19 may progress to severe disease in high-risk patients and patients of the second wave were older and respiratory distress was more frequent, health indicators improved in the second wave of the pandemic.

### Authors' Contributions

Conception of the study: Francisco Gude, Luis Valdés.

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Data collection: Nuria Rodríguez-Núñez, Adriana Lama, Carlos Rábade, Alfonso Varela, Romina Abelleira, Ana Casal, Vanessa Riveiro, Manuel Taboada.

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Drafting the manuscript: All authors helped to revise the draft of the manuscript.

Editing and approval of the manuscript: All authors.

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### Conflict of Interest

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