Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

Infection with the Omicron variant of SARS-CoV-2 is associated with less severe disease in hospitalized patients with COVID-19

Dear editor,

We read with interest a recent letter by Lippi and colleagues, who suggest that Sars-Cov-2 Omicron variant causes less severe illness compared to outbreaks with previous strains.[1] The evolution of SARS-CoV-2 has led to several variants, each one with its own characteristics. Therefore, monitoring the potential implications of these new variants in terms of virulence or transmissibility is of the utmost importance. Omicron was considered a variant of concern (VoC) by the World Health Organization (WHO).[2] Due to the high number of mutations on the spike protein and its increased transmissibility, Omicron has become the predominant variant worldwide in a remarkably short time.[3,4] Similar to other regions, the emergence of the Omicron variant in Spain coincided with a record number of patients diagnosed with COVID-19.[5] However, the percentage of patients infected in the community who required hospital admission has been lower than in previous waves. Data on the characteristics and outcomes of patients hospitalized with this new variant could help define the most appropriate epidemiological measures and treatment protocols to address breakthrough scenarios.

Here, we present a detailed description of the clinical characteristics, viral load, frequency of inflammatory phenotype, and outcomes in hospitalized patients with SARS-CoV-2 infection caused by the Omicron variant, comparing these data with previous admissions.

We included all consecutive adults hospitalized at the Hospital Clinic of Barcelona >48 hours for SARS-CoV-2 infection between February 19th, 2020 and February 24th, 2021, presumably alpha and beta variants. We then compared with the first 90 patients both hospitalized in our center and identified with SARS-CoV-2 caused by the Omicron variant.

During the first peak of the pandemic (March-April 2020), COVID-19 diagnoses (hereafter referred to as the Non-Omicron group) were confirmed by real-time polymerase chain reaction (RT-PCR) testing performed on nasal and oropharyngeal throat-swabs, and/or by clinical diagnostic criteria for SARS-CoV-2. The Omicron variant was identified through a multiplex RT-PCR Allplex SARS-CoV-2 Variants I assay and II assay (Seegene Inc., Korea).

This study was approved by the Institutional Ethics Committee of the Hospital Clinic of Barcelona, which waived individual patients' consent for the retrospective data review (HCB/2020/0273).

We retrieved high-quality data from electronic health records on demographic characteristics, clinical signs, laboratory tests, microbiological results, treatments, and outcomes.

We defined four clinical phenotypes: viral, inflammatory, co-infection and thrombotic. The viral phenotype comprised patients with a cycle threshold (Ct) value of less than 28 in RT–PCR at COVID-19 diagnosis. The inflammatory phenotype comprised patients with a C-RP higher than 8 mg/dL and/or ferritin higher than 1000 ng/mL and/or LDH higher than 320 U/L. The co-infection phenotype comprised patients with clinically suspected co-infection, given procalcitonin levels being higher than 0.2ng/mL. Finally, the thrombotic phenotype comprised patients with D-dimer levels higher than 1000 ng/mL. Patients may have one or more of these phenotypes at the same time.

Categorical variables were described using the absolute number and percentage, while continuous variables were presented using the median and interquartile range (IQR). Categorical variables were compared using either a chi-squared (χ^2) test and quantitative variables with the Mann-Whitney U test. Analyses were performed using Microsoft SPSS-PC+, version 22.0 (SPSS, Chicago, IL, USA).

We included 3224 adults (3134 in the non-Omicron group and 90 in the Omicron group) in the study. In the Omicron group, 84% of patients had been vaccinated; 2.2% had had a COVID-19 episode.

Table S1 summarizes these patients' epidemiological, clinical characteristics, treatment and outcomes. Data for SARS-CoV-2 PCR Ct value was available in 1573 patients, of whom 1507 belonged to the non-Omicron group and 66, the Omicron group. A viral phenotype with a Ct value of under 28 presented in a total of 97% vs 61.8% ($p<0.001$) in the Omicron and non-Omicron groups, respectively. An inflammatory phenotype was present in 48 of 90 (53.3%) patients in the Omicron group and 2096 of 3080 (68.1%) patients in the non-Omicron group ($p = 0.003$). Specifically, when comparing the non-Omicron and Omicron groups, elevated C-RP, ferritin and LDH were documented in 49.6% versus 33.3% ($p = 0.002$); 33.1% versus 18.3% ($p = 0.009$); and 44.8% versus 33.3 ($p = 0.041$), respectively. A co-infection phenotype was present in 50% of patients belonging to the non-Omicron group and 31% of patients belonging to the Omicron group ($p = 0.001$).

Table S2 details data on patients with specific characteristics (immunocompromised status, and either Intensive Care Unit (ICU) or conventional ward admission).

This study compared the epidemiological characteristics and clinical picture of patients diagnosed with the Omicron variant to those infected by COVID-19 in earlier waves. Most patients in the Omicron group were older, they had mores comorbidities and less systemic inflammation and often presented bacterial co-infections. Also immunocompromised patients were admitted for early treat-

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ment to minimize the likelihood of progression to severe COVID-19. In both clinical situations, respiratory failure was infrequent and pro-inflammatory phenotype uncommon. To date, we have not hospitalized any patient with the Omicron variant presenting without comorbidities and under the age of 70 years who required mechanical ventilation or died. Our results are consistent with previous population-based studies documenting better outcomes in patients infected with the Omicron variant.[6–9]

A plausible, biological explanation of our results is that the Omicron variant replicates faster than all other SARS-CoV-2 variants in the upper respiratory tract, but it multiplies less efficiently in the lung parenchyma.[10] Due to its high affinity for the upper airway, it is unlikely that the Ct values detected in PCRs of nasopharyngeal samples from Omicron patients will provide us with the same information compared to previous waves.

The high number of older patients in the Omicron group may also explain the mortality rate documented in subjects with this variant.

Finally, hospitalized patients with SARS-CoV-2 Omicron infection had a different clinical picture: most were older and immunocompromised and had comorbidities. Clinical characteristics showed high viral burdens in the nasopharynx and a low systemic inflammatory response. Fever and respiratory failure were less frequent.

As long as the Omicron variant remains predominant, we recommend that epidemiological and treatment protocols should be adjusted to lower the risk of progression to respiratory failure and death.

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Data availability statement

The authors confirm that the data supporting the findings of this study are available within the article and its supplementary materials.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jinf.2022.07.029.

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Tommaso Francesco Aiello[#*], Pedro Puerta-Alcalde, Mariana Chumbita, Patricia Monzó, Carlos Lopera
Infectious Diseases Department, Hospital Clinic of Barcelona-IDIBAPS, Universitat de Barcelona, C/ Villarroel 170, Barcelona 08036, Spain

Juan Carlos Hurtado
Microbiology Department, Hospital Clinic, University of Barcelona, ISGLOBAL, Barcelona, Spain

Fernanda Meira
Infectious Diseases Department, Hospital Clinic of Barcelona-IDIBAPS, Universitat de Barcelona, C/ Villarroel 170, Barcelona 08036, Spain

Mar Mosquera, Marta Santos, Mariana Fernandez-Pittol
Microbiology Department, Hospital Clinic, University of Barcelona, ISGLOBAL, Barcelona, Spain

Josep Mensa, José Antonio Martínez, Alex Soriano
Infectious Diseases Department, Hospital Clinic of Barcelona-IDIBAPS, Universitat de Barcelona, C/ Villarroel 170, Barcelona 08036, Spain

Ma Angeles Marcos
Microbiology Department, Hospital Clinic, University of Barcelona, ISGLOBAL, Barcelona, Spain

Carolina Garcia-Vidal[*,#]
Infectious Diseases Department, Hospital Clinic of Barcelona-IDIBAPS, Universitat de Barcelona, C/ Villarroel 170, Barcelona 08036, Spain

[*]Corresponding authors.
E-mail addresses: tfaiello@clinic.cat (T.F. Aiello), cgarciav@clinic.cat (C. Garcia-Vidal)
[#] Authors Tommaso Francesco Aiello and Carolina Garcia-Vidal contributed equally to this manuscript.