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## Clinical report

Clinical characteristics of children hospitalized for COVID-19<sup>☆</sup>

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## ABSTRACT

**Introduction:** Most SARS-CoV2 infections in the pediatric population are asymptomatic or with mild symptoms, with a minimal proportion of severe cases described as SARS-CoV2-associated multi-system inflammatory syndrome (MIS-C).

The objective was to describe the clinical and epidemiological characteristics of pediatric patients admitted with confirmed diagnosis of SARS-CoV2 infection from the beginning of the pandemic until May 2021.

**Methods:** Retrospective observational study of pediatric patients hospitalized with confirmed COVID-19, in a tertiary hospital. Epidemiological and clinical data, additional tests, treatments administered and evolution were collected.

**Results:** 30 patients were included, classified into 3 groups according to diagnosis: respiratory infection, MIS-C and compatible symptoms. The patients with pneumonia were associated with age older, comorbidities and lymphopenia. MIS-C were more serious patients, with marked laboratory involvement and greater admission to PICU. Most of these were secondary cases of contact in the family environment.

**Discussion:** The most frequent clinical manifestations of COVID-19 in children are mild-moderate respiratory with good evolution. MIS-C is another form of expression of SARS-CoV2 infection of greater severity, but usually with good prognosis after early diagnosis and frequent PICU admission.

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## Características clínicas de los niños hospitalizados por COVID-19

## RESUMEN

**Introducción:** La mayoría de infecciones por SARS-CoV2 en población pediátrica cursan asintomáticas o con síntomas leves, con porcentaje mínimo de casos graves descritos como síndrome inflamatorio multisistémico asociado al SARS-CoV2 (SIM-PEDs).

El objetivo fue describir las características clínico epidemiológicas de aquellos pacientes pediátricos ingresados, con diagnóstico confirmado de SARS-CoV2 desde el inicio de la pandemia hasta mayo 2021.

**Métodos:** Estudio retrospectivo observacional de pacientes pediátricos ingresados con diagnóstico de COVID-19, de un hospital terciario. Se recogieron datos demográficos, clínicos, pruebas complementarias, tratamiento administrado y evolución.

**Resultados:** Se incluyeron 30 pacientes, clasificándose en 3 grupos según diagnóstico: Infección respiratoria, SIM-PEDs y síntomas compatibles. Los pacientes con neumonía asociaban mayor edad, comorbilidades y linfopenia. SIM-PEDs fueron pacientes más graves, con afectación analítica marcada y mayor ingreso en UCIP. La mayoría eran casos secundarios de contacto en el entorno familiar.

**Discusión:** Los cuadros clínicos de COVID-19 más frecuentes en niños son respiratorios leves-moderados con buena evolución. SIM-PEDs es otra forma de expresión de infección por SARS-CoV2 de mayor gravedad, pero habitualmente con buen pronóstico tras diagnóstico precoz y requiriendo frecuentemente ingreso en UCIP.

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## Introduction

The lesser severity of the 2019 coronavirus disease (COVID-19) in the pediatric population has been evident since its declaration as a global pandemic by the World Health Organization (WHO).<sup>1</sup>

During the first period of this global crisis, pediatric care in Madrid (Spain) was centralized in two tertiary hospitals with a view to optimize resources due to the high healthcare demand of the adult population. This specialized care subsequently returned to normal during the following waves of the pandemic.

According to reports issued by the Spanish Epidemiological Surveillance Network (RENAVE, *Red Nacional de Vigilancia Epidemiológica*), the incidence of pediatric cases raised (19.4%) as a result of the increase in diagnostic testing in this patient population, but no increase in the severity of the condition was observed. In fact, only 0.6% of pediatric cases had to be hospitalized, with just 5.2% of these patients requiring admission to the intensive care unit (ICU).

Furthermore, less than 0.6% of hospitalized pediatric patients have passed away since the beginning of the pandemic.<sup>2</sup>

Fortunately, most pediatric cases are asymptomatic or mild,<sup>1</sup> although a small percentage of cases can develop severe acute respiratory syndrome coronavirus 2-related multisystem inflammatory syndrome in children (MIS-C).<sup>3</sup> The clinical variability of these patients is such that their treatment will depend on the type of presentation.<sup>4</sup>

The aim of this study was to describe the clinical and epidemiological characteristics of the pediatric patients who were admitted to our hospital with a confirmed diagnosis of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection from the beginning of the pandemic until May 2021.

## Methods

This was a retrospective, observational study including all patients under the age of 18 who were admitted to the Pediatric Unit of a tertiary hospital with a diagnosis of COVID-19. All cases were classified into three diagnostic groups: respiratory tract infection, MIS-C, and a third group of miscellaneous diagnoses (compatible symptoms not attributable to the other two diagnoses).

The following variables were collected: patients' demographic characteristics, personal history, clinical manifestations at admission, and diagnostic-therapeutic procedures.

The study inclusion criteria were as follows: patients under the age of 18 who had been admitted to the hospital between 1 March 2020 and 31 May 2021 with an acute SARS-CoV-2 infection confirmed by a positive polymerase chain reaction (PCR) test or clinical manifestations compatible with a positive serology for SARS-CoV-2. The method used to detect antibodies against the virus was Abbot's SARS-CoV-2 IgG II Quant immunoassay. The method used to detect the SARS-CoV-2 was a PCR test performed on a sample of nasopharyngeal aspirate.

The study was approved by the Ethics Committee.

All statistical analyses were carried out using the SPSS 2021 software. Qualitative variables are presented as frequencies and percentages according to each category. Quantitative variables without a normal distribution are presented as a median and interquartile range (IQR). Qualitative variables were compared with each other using contingency tables, Fisher's statistical test, and, subsequently, the chi-squared test, with results being considered statistically significant when the p-value was below 0.05.

## Results

A total of 30 patients were included in this study. Tables 1 and 2 show the main characteristics of these patients. Up to 56.7% of these patients corresponded to secondary cases resulting from a close contact within the family setting. Five patients (16.7%) had to be admitted to the pediatric ICU (PICU), and none of the passed away. Four of these patients had MIS-C and one had severe asthma.

A total of 18 patients (60%) were admitted to the respiratory tract infection group. Ten of them (55.5%) had pulmonary infiltrates revealed by a chest X-ray. In addition, a greater number of comorbidities (asthma, immunosuppression, cerebral palsy, and obesity) was recorded in this subgroup, in addition to a tendency toward an association between older age and pneumonia compared with the other diagnoses ( $P=.09$ ), excluding the MIS-C group. Eighty percent (80%) of the patients who had associated pneumonia were of Latin American origin. Only one (5.6%) patient with a history of asthma had to be admitted to the PICU due to developing severe bronchospasm. The most frequent symptoms were fever (77.8%) and cough (72.2%), followed in frequency by dyspnea (55.6%), with no differences between patients with and without associated pneumonia.

At an analytical level, the blood work revealed an association between lymphopenia and pneumonia, although without reaching statistical significance ( $P=.06$ ).

The MIS-C group included five patients (16.7%), four (80%) of whom were transferred from another hospital to be admitted to the PICU of our center. The median age of these patients was 10 years (IQR 9.02–13.2 years) and 80% were also of Latin American origin. The predominant symptoms in all of these patients were fever, digestive symptoms, and, to a lesser extent, conjunctival hyperemia and headache.

At an analytical level, a higher incidence of lymphopenia (60%) and increased inflammatory marker levels were observed with respect to the other diagnostic groups.

In the third group, which included patients with compatible symptoms not attributable to the other two diagnoses, data from a total of seven patients (23.3%) with a median age of 0.84 years (IQR 0.02–17.07 years) were collected. These patients had few analytical alterations and only required symptomatic treatment.

Tables 3 and 4 summarize the clinical, analytical, and radiological characteristics of these patients and the treatments administered.

## Discussion

The results of our study confirm the mild severity of SARS-CoV-2 infections in most children requiring hospital admission.

Although the incidence of SARS-CoV-2 infection in children is slightly lower than in adults, patients <14 years account for 12% of infections in our country.<sup>2</sup>

As this infection is milder in the pediatric population, determining the potential severity risk factors in children, such as the presence of comorbidities, is necessary.<sup>5</sup>

It is also important to establish the characteristics of the MIS-C, as this condition can be extremely severe and be linked to increased morbidity. A systematic review on the cardiovascular impact of this disease on the European and North American populations presenting with this diagnosis (688 cases recorded between April and July 2020) revealed a 73% incidence of ICU admission, with 54% of cases developing cardiogenic shock, 15% coronary abnormalities, and 1.7% resulting in death.<sup>6</sup>

The clinical manifestations of SARS-CoV-2 infections vary greatly, with fever, respiratory manifestations, and digestive symptoms predominating in our cohort, in line with that reported in

**Table 1**  
Epidemiological characteristics categorized by diagnostic groups and overall.

Characteristics	Respiratory tract infection (n = 18)	MIS-C (n = 5)	Compatible symptoms (n = 7)	Total (n = 30)
Age (years)	5.32 (0.24–15.49)	10.07 (9.02–13.2)	0.84 (0.02–17.07)	9.16 (0.24–15.35)
Median (IQR)				
Male, N (%)	9 (50%)	2 (40%)	2 (28.6%)	13 (43.3%)
Comorbidities, n (%)	7 (38.8%)	1 (20%)	2 (28.5%)	10 (33.3%)
<i>Source, N (%):</i>				
Emergency Department	14 (77.8%)	1 (20%)	5 (71.4%)	20 (66.6%)
Other hospital	4 (22.2%)	4 (80%)	2 (28.6%)	10 (33.3%)
ICU admission	1 (5.6%)	4 (80%)	0	5 (16.7%)
<i>Origin, N (%) Spanish/foreigner</i>				
	5 (27.8%)/13 (72.3%)	1 (20%)/4 (80%)	5 (71.4%)/2 (28.6%)	11 (36.7%)/19 (63.3%)
<i>Index case/2nd/unknown</i>				
	11.1%/66.7%/22.2%	0%/60%/40%	42.9%/28.6%/28.6%	16.7%/56.7%/26.7%

**Table 2**  
Patients included in the study categorized by age range and diagnostic group.

	Respiratory infection		MIS-C	Compatible symptoms
	Normal X-ray	Infiltrated X-ray		
0–29 days	1	0	0	2
1–2 months	2	1	0	1
3–35 months	4	1	0	1
3–9 years	0	1	2	0
10–17 years	1	7	3	3
Total	18	5	7	

**Table 3**  
Clinical, analytical, and radiographic characteristics categorized by diagnostic group and overall.

	Respiratory tract infection (n = 18)	MIS-C (n = 5)	Compatible symptoms (n = 7)	Total (n = 30)
<i>Symptoms, N (%)</i>				
Fever	14 (77.8%)	5 (100%)	2 (28.6%)	21 (70%)
Cough	13 (72.2%)	0	0	13 (43.3%)
Dyspnea	10 (55.6%)	0	0	10 (33.3%)
Digestive complaints	7 (38.9%)	5 (100%)	3 (42.9%)	15 (50%)
Skin desquamation	0	1 (20%)	0	1 (3.3%)
Conjunctival hyperemia	1 (5.6%)	3 (60%)	0	4 (13.3%)
Headache	3 (16.7%)	2 (40%)	2 (28.6%)	7 (23.3%)
<i>Analytical data</i>				
Lymphopenia	3 (16.7%)	3 (60%)	0	6 (20%)
Altered ferritin	8 (44.4%)	4 (80%)	1 (14.3%)	13 (43.3%)
Altered D-dimer	10 (55.6%)	5 (100%)	2 (28.6%)	17 (56.7%)
Altered pro-BNP	3 (16.7%)	4 (80%)	1 (14.3%)	8 (26.7%)
Altered CRP	9 (50%)	5 (100%)	0	14 (46.7%)
Altered PCT	2 (11.1%)	3 (60%)	0	5 (16.7%)
<i>Image, N/total (%)</i>				
Chest X-ray performed	14/18 (77.7%)	4/5 (80%)	2/7 (28.5%)	20/30 (66.6%)
Altered X-ray	10/14 (71.4%)	0/4 (0%)	0/2 (0%)	10/20 (50%)

Ferritin levels >200 ng/mL, D-dimer levels >500 ng/mL, pro-brain natriuretic peptide (pro-BNP) levels >125 pg/mL, C-reactive protein (CRP) levels >1 mg/dL, and procalcitonin (PCT) levels >0.5 ng/mL.

**Table 4**  
Treatments administered categorized by diagnostic group and overall.

Treatments	Respiratory tract infection (n = 18)	MIS-C (n = 5)	Compatible symptoms (n = 7)	Total (n = 30)
Oxygen therapy	10 (55.6%)	1 (20%)	0	11 (36.7%)
Corticosteroids	5 (27.8%)	5 (100%)	0	10 (33.3%)
Gamma globulin	0	4 (80%)	0	4 (13.3%)
ASA	0	3 (60%)	0	3 (10%)
LMWH	3 (16.7%)	3 (60%)	0	6 (20%)
Remdesivir	2 (11.1%)	0	0	2 (6.7%)
ABT	2 (11.1%)	4 (80%)	0	6 (20%)
Vasoactive drugs	0	2 (40%)	0	2 (6.7%)

ASA: acetylsalicylic acid. ABT: antibiotic therapy. LMWH: low molecular weight heparin.

other case series.<sup>7</sup> The Spanish Pediatrics Association (AEP, *Asociación Española de Pediatría*) also carried out a systemic review on COVID-19 symptoms for which they selected 18 studies, most of which were carried out in a hospital setting. In line with that observed in the present study, fever was the most frequent (56.5%) symptom identified in all of these studies. The next most frequent

symptoms were cough (45.7%), respiratory distress (27.9%), and digestive disorders (24.1%).<sup>8</sup>

A remarkable finding of our study is that children presenting with lobar condensations were older (8–16 years) and many had comorbidities: asthma, obesity (body mass index [BMI] >33 kg/m<sup>2</sup>), or immunosuppression. Furthermore, 80% of them were of Latin

American origin, which is a noteworthy finding, as only 11.1% of the pediatric patients who were cared for at our Emergency Room during said period were foreigners.

On the other hand, 16% of the hospitalized patients in our case series were diagnosed with MIS-C, which is a much higher percentage than that described in the literature, a fact that could be explained by the referral of patients requiring ICU admission from other areas. Although all patients exhibited a good clinical evolution without sequelae, the early recognition of this clinical picture is of vital importance owing to the risk of severe complications, particularly of cardiac nature (systolic dysfunction, coronary aneurysms, etc.).<sup>9</sup> As this condition corresponds to a hyperresponse of the immune system several weeks following the infection, it requires immunomodulatory treatment, including the administration of intravenous gamma globulin and/or corticosteroids.

The presentation of this condition in children under the age of one, despite being mild,<sup>7</sup> is associated with a greater degree of hospitalization for their close monitoring.<sup>10</sup> This was seen in our own patient sample, with two newborns being admitted preventatively despite being asymptomatic.

Unlike adults, pediatric patients generally have a lower rate of analytical alterations, the most common ones being lymphopenia and increased inflammatory marker levels. However, these alterations are more striking among patients with MIS-C. The data available in the literature are disparate due to the variability of criteria applied to the conduct of blood work, as this test is routinely not recommended in the case of patients being followed on an outpatient basis. In line with our study observations, another Spanish case series including hospitalized patients revealed a greater percentage of lymphopenia and increased inflammatory marker levels correlating with the severity of the patients' condition.<sup>5</sup>

The limitations of our study are, among others, its retrospective nature and small sample size, mainly owing to the following two reasons: the low number of admissions during the first period of the pandemic due to the centralization of the pediatric care, and the subsequent outpatient management of the vast majority of patients due to the low severity of their condition.

Since our hospital attends a very heterogeneous population and our PICU is a referral unit for several peripheral hospitals, the percentage of critically ill patients included in our sample was higher than usual; therefore, it cannot be extrapolated. Moreover, our admission criteria varied over the months as the overall understanding of the disease increased. A very important change occurred between the first wave of the pandemic and the following ones, since the availability of diagnostic PCR testing in the Emergency Department was extended to all children with symptoms compatible with this infection.

As for the strengths of our study, all patients were included consecutively, thus preventing any selection bias. The diagnosis of SARS-CoV-2 infection was reached through a PCR test, which is the most sensitive test available to confirm this disease, or the presence of MIS-C criteria. Considering the scarce literature available on this infection in children, we believe that we provide a representative case series of the pediatric population, in addition to relevant information on the natural history of the disease and a wide range of its clinical manifestations.

In conclusion, the most frequent clinical manifestations of COVID-19 in children requiring hospitalization are mild-moderate respiratory symptoms exhibiting a good clinical evolution. A more

severe presentation of SARS-CoV-2 infection is MIS-C, although this condition tends to evolve well following supportive therapy and treatment in the ICU. More studies are needed on the evolution and risk factors for admission or severity of this condition in the pediatric population in order to enable a more individualized approach.

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## Conflicts of interest

The authors declare no conflicts of interest.

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