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Comparison of pneumonia features in children caused by SARS-CoV-2 and other viral respiratory pathogens

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Abstract

Background: Pneumonia is a frequent manifestation of coronavirus disease 2019 (COVID-19) in hospitalized children.

Methods: The study involved 80 hospitals in the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Spanish Pediatric National Cohort. Participants were

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children <18 years, hospitalized with SARS-CoV-2 community-acquired pneumonia (CAP). We compared the clinical and radiological characteristics of SARS-CoV-2-associated CAP with CAP due to other viral etiologies from ValsDance (retrospective) cohort.

Results: In total, 151 children with SARS-CoV-2-associated CAP and 138 with other viral CAP were included. Main clinical features of SARS-CoV-2-associated CAP were cough, fever, or dyspnea. Lymphopenia was found in 43% patients and 15% required admission to the pediatric intensive care unit (PICU). Chest X-ray revealed condensation (42%) and other infiltrates (58%). Compared with CAP from other viral pathogens, COVID-19 patients were older, with lower C-reactive protein (CRP) levels, less wheezing, and greater need of mechanical ventilation (MV). There were no differences in the use of continuous positive airway pressure (CPAP) or HVF, or PICU admission between groups.

Conclusion: SARS-CoV-2-associated CAP in children presents differently to other virus-associated CAP: children are older and rarely have wheezing or high CRP levels; they need less oxygen but more CPAP or MV. However, several features overlap and differentiating the etiology may be difficult. The overall prognosis is good.

KEYWORDS
chest X-ray, clinical features, pneumonia in children, SARS-CoV-2, severity

1 | INTRODUCTION

Community-acquired pneumonia (CAP) is one of the most frequent infectious diseases in children, leading to widespread antibiotic use and hospitalization. Although CAP is often multifactorial, viruses, including respiratory syncytial virus (RSV), human metapneumovirus (hMPV), influenza, parainfluenza virus (PIV), rhinovirus (RhV), and adenovirus (ADV), are considered the main causative agents of pediatric CAP worldwide, with a reported rate of 25%–82%.[1–4]

Similar to other viruses of the coronavirus family, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes a spectrum of clinical manifestations grouped under the term coronavirus disease 2019 (COVID-19), and patients often present with respiratory conditions of different severity, including CAP. Children usually have a less severe COVID-19 infection than adults[2–9] and <15% require hospitalization.[5–8] Among hospitalized children, however, the most frequent diagnosis is CAP.

We recently showed that COVID-19 positivity by real-time PCR (RT-PCR) in children can persist for up to 3 months.[9] It should be considered that SARS-CoV-2 infection in children can even be asymptomatic, and that a positive PCR could be from a recent infection a few weeks or even months ago.

At present, as the virus is so widespread in the community, when faced with a child with CAP and a positive RT-PCR for SARS-CoV-2, we should not automatically exclude the possibility of other viral pathogens causing the pneumonia. It remains unclear whether SARS-CoV-2-associated CAP can be differentiated from other viral CAP-related infections based on clinical, analytical, or radiographical findings. Furthermore, in children with CAP and coinfections with SARS-CoV-2 and other viruses, it is difficult to distinguish which virus contributes most to the CAP.[10] Therefore, it would be important to consider and detect other possible coinfections in these patients.

The present study aims to determine the characteristics of children admitted due to SARS-CoV-2-associated CAP and to compare these findings with those of children with other viral-associated CAP.

2 | MATERIALS AND METHODS

2.1 | Patients

The Epidemiological Study of Coronavirus in Children (EPICO-AEP) is a prospective multicenter national study conducted in Spain, to assess the characteristics of children with COVID-19. In the present study, we included hospitalized children with a primary diagnosis of SARS-CoV-2-associated pneumonia enrolled in EPICO-AEP. CAP was defined as cough and/or respiratory symptoms, and an image consistent with pneumonia in the chest X-ray (CXR),[11] according to the criteria applied by the attending physician. COVID-19 infection was confirmed by RT-PCR testing

or by rapid antigen detection testing on nasopharyngeal swabs. We enrolled pediatric patients (ages 18 years and younger) from 80 hospitals of the network, from February 25, 2020 to April 30, 2021.

Epidemiological, clinical, laboratory, and radiological data were collected from medical records, including the age at onset of the infection, sex, clinical signs and symptoms, outcomes, laboratory data, CXR findings, comorbidities, treatment, and pediatric intensive care unit (PICU) admission. Radiographs were obtained following the institutional protocols of each participating center and all included patients underwent at least one CXR. The interpretation of the CXR was performed following the standards of the "WHO Vaccine Trial Investigators Radiology Working Group."[12] These standards establish two possible interpretations: primary endpoint pneumonia (the presence of consolidation, infiltrate, or pleural effusion), which we will call "consolidation" henceforth, and "other infiltrates."

We used a standardized data collection online platform (Research Electronic Data Capture: RedCAP™) to record and collect the clinical data.

The findings were compared with retrospective data from children diagnosed with viral-associated CAP from a different study performed by our group.[13] In this study (ValsDance cohort), eligible participants were children under 18 years of age, admitted to any of the participating hospitals, with radiologically confirmed CAP, from April 2012 to May 2019. An extensive microbiological workup was performed, including blood cultures, *Streptococcus pneumoniae* antigen (BinaxNow™) and/or RT-PCR for *S. pneumoniae* in pleural fluid if thoracentesis was performed, RT-PCR in blood for *S. pneumoniae*, multiplex RT-PCR on nasopharyngeal aspirate samples for pertussis and for the following panel of 16 viruses: RSV, hMPV, PIV 1, 2, 3, and 4, influenza (A and B), human bocavirus (hBoV), ADV, enterovirus (EV), RhV, and coronavirus (CoV) 229E, OC43, NL63, and HKU12. Two paired samples for serology (at admission and 2–4 weeks later) for *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* were performed using enzyme-linked immunoassays.[14]

Viral etiology was assigned to CAP if at least one putative pathogen respiratory virus (RSV, influenza A or B, PIV, hMPV) was detected in nasopharyngeal aspirates by PCR and no bacterial pathogen was detected. Other respiratory viruses (RhV, ADV, EV, CoV, hBoV) were not included as likely viral infections due to poor specificity for CAP.[15,16]

Both studies were approved by the ethics committee of every center and all guardians signed the informed consent to participate in the study.

2.2 | Statistical analysis

Data were described with frequencies for categorical variables and means (SD) or medians (interquartile range [IQR]) for continuous variables (depending on normal or non-normal distribution), both in the total population and stratified by type of pneumonia (Table 1). Then χ^2 or Fisher's tests were applied to assess differences across groups for categorical variables and Student's *t* test or the Mann–Whitney *U* test was used for continuous variables. Two-tailed $p < 0.05$ was considered statistically significant.

Univariable comparisons were segmented by the presence (Yes) or absence (No) of patients' features among children with SARS-CoV-2 CAP and other viral CAP. We also performed univariate comparisons for different outcome endpoints (admission to PICU, complications, and so on, to test for differences between patients with COVID-19 CAP or other virus-associated CAP. The latter analysis consisted of stepwise multivariable binary logistic regression, with the endpoint being PICU admission (Table 2). The multivariable model was adjusted by type of pneumonia, sex, age (years), asthma, respiratory rate, oxygen saturation, wheezing, shortness of breath or work breathing, radiological image interpretation, leukocytes, C-reactive protein (CRP), neutrophils, lymphocytes, sodium, albumin, procalcitonin, and hemoglobin. The optimum model was selected according to Akaike Information Criteria.

REDCap data were exported to the R language (4.0.3)[17] for analysis. R packages were used for specific analysis, such as compare Groups (4.4.6) for comparisons or MASS (7.3.53) for stepwise logistic regression.

3 | RESULTS

As of April 30, 2021, the EPICO-AEP database had registered 666 hospitalized patients, including 165/666 (25%) with a final diagnosis of CAP at discharge. Of the 165 patients, 151 with pathological CXR on admission were selected for the comparative study.

For analytical purposes, the patients were distributed according to the COVID-19 waves. Until the end of April 2021, Spain experienced four waves (Figure 1): first wave, February 27 to May 31, 2020; second wave, June 1 to November 2, 2020; third wave, September 15 to December 15, 2020; fourth wave, December 15, 2020 to April 30, 2021. The maximum peak of admissions for CAP was recorded during the first wave: with 83% of cases (126/151).

3.1 | Clinical features and outcomes of patients with SARS-CoV-2-associated pneumonia

Demographic and clinical characteristics are shown in Table 1. A total of 76/151 (50%) children had household contact with a confirmed COVID-19 patient. Almost half (72/151, 48%) of all children in our series had underlying conditions, including the following: asthma, 29/144 (20%); immunosuppressive treatment, 22/151 (14%); chronic lung disease, 16/151 (11%); or heart disease, 15/151 (10%). Of the 151 patients, 22 (15%) required admission to a PICU, during a median of 5 days (IQR: 1–15). Most children (146/151, 97%) had a favorable clinical course and were discharged after improvement. However,

TABLE 1 Basal features and risk of SARS-CoV-2-associated CAP.

	Other viruses (*n* = 138)	COVID-19 (*n* = 151)	OR	p. overall
Demographics characteristics				
Age (years), median (range)	1.0 [0.25;2.75]	8.00 [1.00;13.00]		**<0.001**
Sex at birth, *n* (%) (*N* = 289)				0.165
Female	67 (48.6)	60 (39.7)	Ref.	
Male	71 (51.4)	91 (60.3)	1.43 [0.90;2.29]	
Previous asthma: yes (*N* = 282)	22 (15.9)	29 (20)	1.33 [0.72;2.47]	0.447
Immunodeficiency: yes (*N* = 289)	0 (0)	22 (14.5)		
CXR imaging features (*N* = 289)				**<0.001**
Condensation, *n* (%)	89 (64.5)	64 (42.4)	Ref.	
Other infiltrates, *n* (%)	49 (35.5)	87 (57.6)	2.46 [1.53;3.98]	
Clinical characteristics, median (range)				
Admission days (*N* = 252)	5.00 [4.00;6.00]	4.00 [3.00;8.00]	1.01 [0.98;1.04]	0.634
Fever days (*N* = 252)	4.00 [1.00;6.00]	5.00 [3.00;8.00]	1.16 [1.08;1.26]	**<0.001**
Temperature (°C) (*N* = 276)	39.00 [38.4;39.70]	37.80 [36.70;38.50]	0.35 [0.26;0.46]	**<0.001**
Respiratory rate (r.p.m.) (*N* = 208)	42 [33.50;51.50]	30 [24.00;42.00]	0.96 [0.94;0.98]	**<0.001**
Oxygen saturation (%) (*N* = 279)	93.0 [90.0;95.0]	97.0 [94.0;98.0]	1.27 [1.18;1.38]	**<0.001**
Clinical characteristics, *n* (%)				
Cough: Yes (*N* = 289)	126 (91.3)	117 (77.5)	0.33 [0.16;0.66]	**0.002**
Chest pain: Yes (*N* = 258)	8 (5.8)	21 (13.9)	3.39 [1.48;8.54]	**0.006**
Wheezing: Yes (*N* = 288)	74 (53.6)	26 (17.2)	0.18 [0.11;0.31]	**<0.001**
Shortness of breath: Yes (*N* = 276)	114 (82.6)	63 (41.7)	0.18 [0.10;0.31]	**<0.001**
Abdominal pain: Yes (*N* = 263)	6 (4.3)	16 (10.6)	3.17 [1.24;9.23]	**0.024**
Vomiting/nausea: Yes (*N* = 287)	52 (37.7)	34 (22.5)	0.49 [0.29;0.82]	**0.009**
Anosmia/dysgeusia: Yes (*N* = 289)	0 (0)	5 (3)		
Laboratory data, median (range)				
Leukocytes ($\times 10^9$/L) (*N* = 272)	11.0 [8.29;15.10]	7.78 [4.60;11.41]	0.94 [0.90;0.98]	**<0.001**
Neutrophils ($\times 10^9$/L) (*N* = 272)	6.70 [4.10;9.67]	3.86 [1.73;7.07]	0.90 [0.85;0.95]	**<0.001**
Lymphocytes ($\times 10^9$/L) (*N* = 272)	2.70 [1.90;4.40]	1.89 [1.05;3.22]	0.83 [0.73;0.93]	**<0.001**
Hemoglobin (g/L) (*N* = 272)	11.60 [10.07;12.50]	12.10 [11.00;13.40]	1.17 [1.02;1.34]	**0.011**
Sodium (mEq/L) (*N* = 256)	137 [135;139]	138 [136;140]	1.12 [1.03;1.22]	**0.039**
Albumin (g/dl) (*N* = 169)	3.70 [3.40;4.10]	3.90 [3.23;4.38]	0.96 [0.58;1.61]	0.390
C-reactive protein (mg/L) (*N* = 272)	48.00 [22.20;116]	21.60 [6.50;67.30]	1.00 [0.99;1.00]	**<0.001**
Procalcitonin (ng/ml) (*N* = 213)	0.33 [0.11;1.19]	0.13 [0.06;0.56]	0.98 [0.92;1.05]	**0.003**

Note: Bold values are statistical significance of $p > 0.05$.

Abbreviations: CAP, community-acquired pneumonia; COVID-19, coronavirus disease 2019; CXR, chest X-ray; OR, odds ratio; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

5/151 (3%) children died and all had serious comorbidities: 3 had chronic lung disease (bronchopulmonary dysplasia, idiopathic interstitial pneumonia, or pulmonary pathology due to spinal muscular atrophy) and 2 had immunosuppression due to hematological disease and bone marrow transplant.

3.2 | Radiology and laboratory findings in SARS-CoV-2-associated pneumonia

For the diagnosis of pneumonia, all patients underwent at least one CXR. Radiological and analytical characteristics are shown in

Table 1. Only a few patients (6/151, 4%) presented with pleural effusion and in 4 of them (4/6: 67%) thoracentesis was performed. Coinfection was demonstrated in only 5 patients (although it was only possible to perform a viral coinfection study for RSV and influenza in 97 cases, 5/97: 5%). Blood culture was done routinely. There were two cases of *Staphylococcus aureus*, one of *S. pneumoniae* (pneumococcal antigen in pleural fluid), and two due to RhV and influenza virus.

TABLE 2 Stepwise multivariable binary logistic regression.

	Coefficient (95% CI)	*p*
Type of pneumonia (COVID-19)	1.91 (0.82–4.58)	0.139
Sex (male)	0.51 (0.21–1.16)	0.115
Asthma (Yes)	2.62 (1.01–6.61)	0.043*
Lymphocytes (mm^3/1000)	0.78 (0.59–0.97)	0.039*
Sodium (mEq/L)	1.16 (1.03–1.32)	0.020*
Hemoglobin (g/dl)	0.70 (0.55–0.88)	0.003**

Note: Endpoint: Admission to PICU. The multivariable model was adjusted by type of pneumonia, sex, age in years, asthma, respiratory rate, oxygen saturation, wheezing, shortness of breath or work breathing, radiological image interpretation, leukocytes, C-reactive protein, neutrophils, lymphocytes, sodium, albumin, procalcitonin, and hemoglobin. The optimal model was selected according to Akaike Information Criteria. Bold entries: Significance codes: *$p < 0.05$; **$p < 0.01$.

Abbreviations: CI, confidence interval; COVID-19, coronavirus disease 2019; PICU, Pediatric intensive care unit.

Full blood count (FBC) analysis revealed leukopenia ($<5 \times 10^9$/L) in 41/142 (29%) cases, lymphocytopenia ($<1.5 \times 10^9$/L) in 59/142 (42%), thrombocytopenia ($<150 \times 10^9$/L) in 22/142 (15%), and anemia (hemoglobin <11.5 g/L) in 54/142 (38%) cases. Regarding inflammatory markers, CRP levels >20 mg/L were reported in 65/135 (48%) patients and procalcitonin levels >0.5 ng/ml in 26/102 (25%), with 12/102 (12%) of the patients having levels >2 ng/ml. Regarding blood coagulation function, the D-dimer median was 699.5 µg/L (IQR: 160.5–3402) and was increased in 62/96 (65%) of the patients.

3.3 | Evolution and treatment in SARS-CoV-2-associated pneumonia

During the admission, 67/151 (44%) patients required oxygen therapy, during a median of 4 days (IQR: 2–28). Regarding respiratory support, 15/151 (10%) required high-flow ventilation (HFV) or continuous positive airway pressure (CPAP); 11/151 (7%) required intubation and mechanical ventilation (MV) during a median of 5 days (IQR: 2–16) and 2/151 (1%) required extracorporeal membrane oxygenation therapy.

Overall, 112/151 (74%) patients received antibiotics, mainly azithromycin (55/112, 49%), ceftriaxone (27/112, 24%), ampicillin (5/112, 4%), or meropenem (6/112, 5%). Antivirals were administered to 67/151 (44%) patients; the most common were remdesivir (12/67, 18%) and lopinavir/ritonavir (10/67, 15%). Other treatments used were hydroxychloroquine in 52/151 (34%)

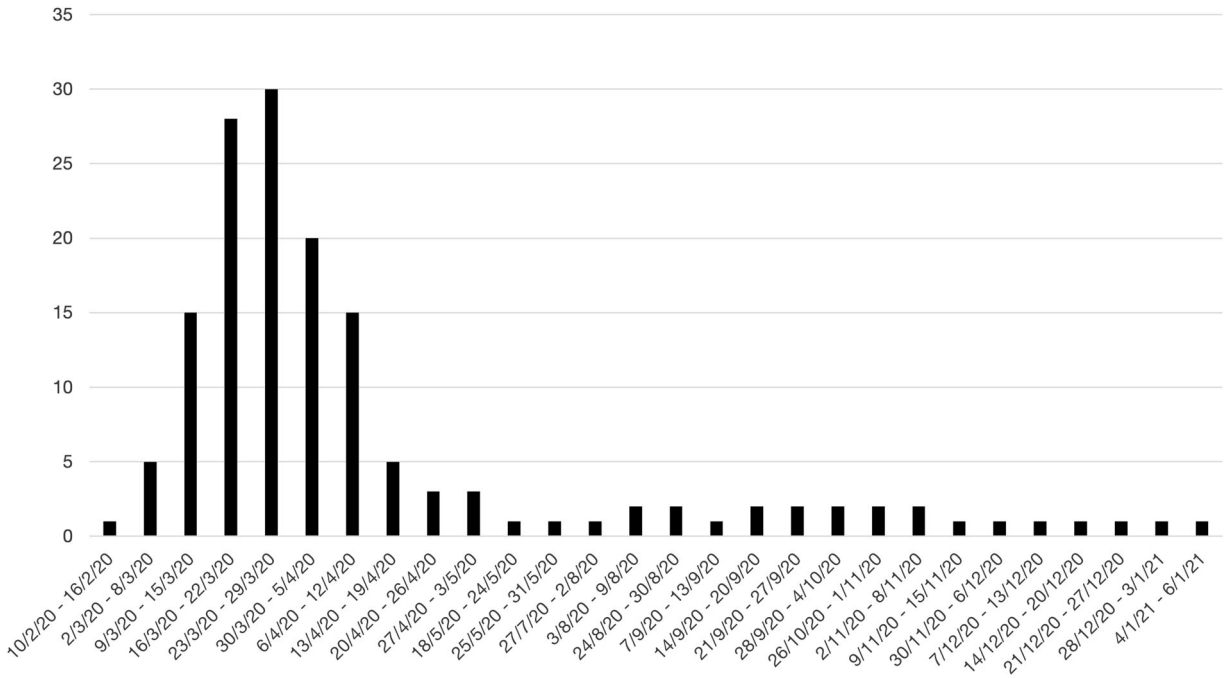

FIGURE 1 Monthly admissions of children with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-associated community-acquired pneumonia (CAP).

patients and immunoglobulins (3/151, 2%) or glucocorticoids (30/151, 20%).

3.4 | Comparison between SARS-CoV-2 CAP and other viral-associated CAP

Unlike the group with SARS-CoV-2-associated CAP, no deaths occurred in the group of other viral-associated CAP.

Compared with patients with other viral-associated CAP, patients with SARS-CoV-2-associated CAP were older, had lower CRP levels, had less wheezing, and had less work of breathing. We found that SARS-CoV-2-CAP was associated with a longer duration of fever but lower degree of fever, and more chest and abdominal pain. These patients also showed more infiltrates on the CRX than in the other viral-associated CAP group (all comparative data can be seen in Table 1).

In terms of treatments, the use of antibiotic therapy is high in both groups (68% vs. 74%). Although the percentage of pleural effusion was higher in the other viral-associated CAP (6% vs. 4%), less corticosteroid therapy (2% vs. 20%) was used than in the SARS-CoV-2-associated CAP group.

Use of oxygen therapy was more frequent in the other viral-associated CAP group (76.8% vs. 44%; odds ratio [OR]: 0.24; 95% confidence interval [CI]: 0.14;0.40, $p < 0.001$).

Conversely, patients with COVID-19 had more cardiological complications, including myocardial dysfunction, shock, or arrhythmia (16.6% vs. 8.7%, OR: 2.08 [95% CI: 1.01;4.3], $p = 0.049$) and more need of MV (7% vs. 0.7%, OR: 10.8 [95% CI: 1.3;85), $p = 0.02$). There were no differences in the use of CPAP or HVF (10% vs. 5.8%, OR: 1.79 [95% CI 0.73–4.3], $p = 0.19$), or PICU admission (15% vs 9%, OR: 1.78 [95% CI: 0.85;3.77], $p = 0.125$; see Figure 2).

The logistic regression model showed that PICU admission was more likely in patients with higher levels of sodium and in patients with prior asthma. Likewise, the odds of PICU admission increased as lymphocytes or hemoglobin decreased (Table 2).

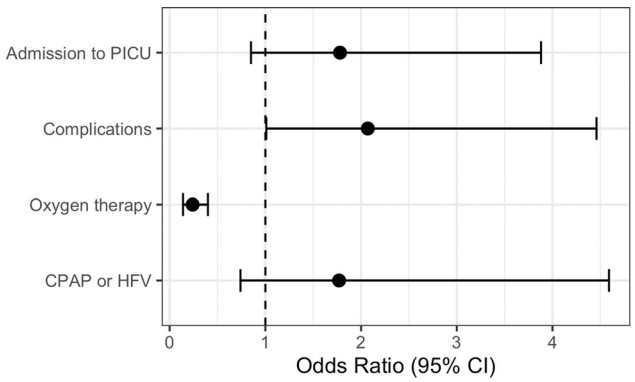

FIGURE 2 Forest plot for the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-associated community-acquired pneumonia (CAP) risk of complications (ref: other viral CAP). CPAP, continuous positive airway pressure; HFV, high flow ventilation; PICU, pediatric intensive care unit.

4 | DISCUSSION

In this study, we compared CAP in patients with SARS-CoV-2 with patients positive for other viral infections. We found that the former was associated with less wheezing and work of breathing, a significantly lower lymphocyte fraction and lower CRP levels. During evolution, the SARS-CoV-2-associated CAP group had significantly higher MV use (almost 10-fold) but less requirement for oxygen. No significant differences were found in terms of days of hospitalization, PICU admission, or CPAP/HFV use.

Several studies have reviewed the characteristics of adults with SARS-CoV-2 and pneumonia,[18–22] but these remain scarce in the pediatric population.[23,24] However, among hospitalized children and adolescents, pneumonia is a major cause of disease (~15%).[5–8]

Similar to other studies,[23,24] the most frequent symptoms in our patients were fever, cough, wheezing, or shortness of breath. We found that SARS-CoV-2-associated CAP occurred in older children (8 years on average, as reported previously),[25] with a longer duration of fever, more cases with chest and abdominal pain, and fewer cases with cough, wheezing, or dyspnea than in non-SARS-CoV-2-associated CAP. Symptoms often overlapped, making it challenging to discern between the two. Given that the median time to RT-PCR negativity for SARS-CoV-2 is 17–19 days, and can remain positive for several weeks up to 3 months,[26,27] a means of differentiating SARS-CoV-2 from other etiologies is important. Children with COVID-19 may be coinfected with other respiratory viruses and/or bacteria. Few studies have reported relevant data on this topic. Similar to other studies,[5] in our series there were 5% of coinfections. The clinical relevance of coinfections is a question that may have important implications. Although further studies are needed to understand the clinical implications of viral coinfections between SARS-CoV-2 and other viruses, investigation of other coinfections could be helpful in the management of these patients.

Many studies evaluating the utility of biomarkers in defining the etiology of pediatric CAP have been performed using FBC, neutrophil percentage, serum CRP, or procalcitonin, although the cutoff points are not well defined. As reported in other studies, we found significant differences in terms of FBC and inflammatory markers,[6,23,24,28] with increased CRP in almost 50% of the patients, but less intense in the SARS-CoV-2 group than in the other viral-CAP group. Some studies have reported very high rates of lymphocytopenia,[6,24] but it appears to be less common in children than in adults.[12,13] Variable lymphocytopenia values have been found in children, between 3% and 33%.[8,22,23,29,30] In our cohort, 42% of the children presented with lymphocytopenia. Both leukocytes and lymphocytes were significantly lower in patients with SARS-CoV-2-associated CAP than in other viral-associated CAP. We have also found that the odds of PICU admission increased as lymphocytes decreased.

The evolution in children was usually good. Mortality in children with SARS-CoV-2-associated CAP is rare, <5% in different series[7,24] (3% in our study), and usually driven by serious comorbidities. About 50% of the EPICO group had underlying conditions: 20% of the

patients had asthma, 11% other chronic lung disease, 14% immunosuppression, and 10% cardiovascular diseases. All five patients who died had underlying conditions. The cohort of patients with other viral-associated CAP excluded patients with immunosuppression, chronic lung disease other than asthma, and hemodynamically significant heart disease. Therefore, appropriate comparison of mortality cannot be performed.

The radiological presentation of SARS-CoV-2 can be nonspecific and indistinguishable from other pathologies. The first published studies of children reported few findings in radiographs;[15] however, subsequent reports have revealed a higher proportion of radiographic abnormalities,[11] which depend on the severity of pulmonary involvement.[31,32] In adults, most computed tomography studies in SARS-CoV-2-associated CAP show ground-glass opacities (25%–60% according to different studies),[33–38] which can progress to white lung. The proportion of white lung in children is low and the mechanism is worth further study. Here, the proportion of other infiltrates was 58%, which might correspond to ground-glass opacities, but they did not often progress to white lung, perhaps because of the limited inflammatory response in children. The proportion of consolidations in SARS-CoV-2-associated CAP (42%) was lower than that found in the other viral-associated CAP group (64%), and again the interpretation is unclear. It might reflect different possible patterns of the infection or different susceptibility to bacterial superinfection. Although bacterial coinfections are frequent in viral CAP,[4,38,39] they were very rare in our cohort (3%). However, a full work-up was not performed for most patients (due to laboratory overload during the pandemic). In some severe cases, pleural effusion may be found but it is rare[10,11,34] (in our series, we found it only in six patients, 4%).

Severe COVID-19 is rare in children, with variable PICU admission rates.[23,24] In our cohort, 15% of children with SARS-CoV-2-associated CAP required PICU admission and, although this was almost double the proportion of the other viral CAP group, the differences were not significant, which may be due to a limited sample size.

Usually, viral-associated CAP in young infants resolves with oxygen therapy or CPAP. The evidence for an effective treatment for SARS-CoV-2 is evolving rapidly. Most reports mention supportive treatment,[12] including oxygen therapy and MV, but MV requirements are highly variable according to different studies in adults (18%–42%[40]). Approximately, half of all our COVID-19 patients required oxygen therapy, up to 10% needed additional noninvasive respiratory support (CPAP, HFV) and 15% required MV. In our cohort, patients with other viral-associated CAP required oxygen more frequently, but SARS-CoV-2-associated CAP had more complications with a greater use of MV. Lung damage associated with SARS-CoV-2 appears different to other viruses, as patients need oxygen less often and MV more often. We hypothesize that part of the respiratory damage is vascular, neuromuscular, or heart-mediated, rather than solely hypoxemia.

Although a high percentage of patients (74%) in our series received antibiotic treatment, it is often not needed in SARS-CoV-2-associated pneumonia, owing to the viral etiology. The reason for this high proportion might lie in the fact that most of our cases were during the first wave of the pandemic when treatment was not yet well established, and by the high percentage of severe cases, as only hospitalized patients were included. Even so, most cases of viral-associated CAP receive antimicrobials at admission.[13] This is a point to be improved in our clinical activity and it would be convenient to carry out other studies focused on this point. It would be important to have a more restrictive attitude regarding antibiotherapy in cases of pneumonia with suspected viral etiology.

Our study has some limitations. First, only hospitalized patients were included and so the results are not representative for ambulatory CAP. Second, some cases had incomplete documentation of the exposure history or clinical features and not all patients underwent a complete blood test or microbiological work-up, due to laboratory overload during the pandemic. The third limitation is the variation in the interpretation of radiographs depending on the observer, which can lead to different interpretations.

A limitation to be taken into account is that in the group of other viral pneumonias, immunosuppression and severe respiratory and hemodynamically significant diseases were the exclusion criteria for the study. This could affect a worse evolution and mortality rate of patients in the SARS-COV-2-associated-CAP group, given that immunosuppressed patients have been shown to be at higher risk in many studies. Likewise, both cohorts were not paired in time, which can complicate the comparability of the results.

5 | CONCLUSIONS

SARS-CoV-2 CAP is associated with more use of advanced respiratory support than other viral-associated CAP and is also related to lower leukocyte and lymphocyte counts, less wheezing or shortness of breath, and lower CRP. There were no differences in the use of CPAP or HVF, days of hospitalization, or PICU admission between groups.

Nevertheless, the overall prognosis is usually good. Although we found some significant differences, many clinical and analytical findings often overlapped. Clarifying the clinical, laboratory, and radiographic characteristics of pediatric patients is important for differential diagnosis of SARS-CoV-2 infection from other viral respiratory infections. Given that PCR can remain positive for some weeks in children with a positive detection of SARS-CoV-2, we should not automatically exclude the possibility of other viral pathogens.

AUTHOR CONTRIBUTIONS

Rut del Valle: Conceptualization (equal); data curation (equal); formal analysis (equal); investigation (lead); resources (equal); supervision (equal); writing—original draft (lead); writing—review and editing (lead). **Álvaro Ballesteros**: Formal analysis (lead); methodology (equal); writing—review and editing (equal). **Cristina Calvo**: Data curation (supporting); supervision (supporting). **Talía Sainz**: Data curation (supporting). **Ana Mendez**: Data curation (equal). **Carlos Grasa**: Data curation (supporting). **Paula R. Molina**: Data curation

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Authors agree to make data and materials supporting the results or analyses presented in their paper available upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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