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Review Article:

Approach to pediatric patients with SARS-CoV2

Abordaje de pacientes pediátricos con SARS-CoV2

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Abstract

The emergence of the SARS-CoV-2 (CoV-2) virus has produced great new challenges for public health and emergency care. The challenges in the Approach to pediatric patients with Sars Cov2, circumscribe changes in the flows of patients, areas of care, and a great training for the appropriate care for patients with the disease caused by this virus (COVID-19). In this research work, an approach to care for children with COVID-19 is described. The information was obtained through national and international guides and the scientific literature obtained through Researchgate, Scielo, PubMed, CDC. Generally speaking, the disease may present as a mild condition of acute upper airway infection or as pneumonia. Approximately 2% cases and close to 2% of all children require admission to the intensive care unit (ICU). There is still no specific antiviral treatment approved for use in children. The indication and choice of antiviral treatment will be agreed with the pediatric infectious disease team and the strategy must be anticipatory; it will be evaluated early and sent to an intensive care unit in cases that require it to avoid complications.

Keywords: SARS-CoV-2; COVID-19; Pediatric Emergency Service.

Resumen

La emergencia del virus SARS-CoV-2 (CoV-2) ha producido nuevos y grandes desafíos para la salud pública y la atención de urgencia. Los desafíos en el abordaje de pacientes pediátricos con SARS-CoV-2 circunscriben cambios en los flujos de pacientes, áreas de atención y una gran capacitación para la atención apropiada a los pacientes con la enfermedad producida por este virus (COVID-19). En el presente trabajo de investigación se describe un abordaje para la atención al niño con COVID-19. La información se obtuvo a través de guías nacionales e internacionales y la literatura científica obtenida a través de Researchgate, Scielo, PubMed, CDC. En términos generales, la enfermedad puede presentarse como un cuadro leve de infección aguda de vías aéreas superiores o como neumonía. Aproximadamente el 2
% casos y cerca al 2 % del total de niños requiere ingreso a la unidad de cuidados intensivos (UCI).
Aún no hay tratamiento antiviral específico aprobado para su uso en niños. La indicación y elección del tratamiento antivírico se consensuará con el equipo de infectología pediátrica y la estrategia debe ser anticipatoria; de forma precoz se evaluará y enviará a una unidad de cuidados intensivos a casos que lo requieran para evitar complicaciones.

Palabras clave: SARS-CoV-2; COVID-19; Servicio de Urgencia Pediátrica.

Introduction

The rapid spread of the coronavirus (SARS-CoV2) that causes severe acute respiratory syndrome (COVID-19) led to a global pandemic. It is estimated that of the total number of infected people, only 2% correspond to pediatric patients (children under 19 years of age)[1].

Since the beginning of the 2019 coronavirus disease pandemic (COVID-19), 4.2 million pediatric cases have been registered in the United States. Most of the cases of COVID-19 in the pediatric population show mild symptoms and close to 2% of all children require admission to the intensive care unit[4]. The role of imaging studies in the initial evaluation, prognosis and progression of patients with COVID-19 (SARS-CoV2) is still an area of study and a discussion factor in the medical community[5,6].

In particular, the virus can cause an infection of the upper and lower respiratory tract that triggers symptoms of mild to severe intensity, especially in individuals with pre-existing diseases such as: diabetes, cancer, immunosuppression, among others[7].

Since the first positive case was reported in Brazil, there has been a progressive increase in cases[8]. In fact, reports from May 30, 2020 highlight Brazil, Peru and Ecuador as the most affected countries. Consequently, the United States[9], in addition to some countries in Europe[10] and Asia,[11] published epidemiological studies of COVID-19 with data from the pediatric population. It is worth highlighting in Latin America studies with data on children and adolescents disclosed by Chile [12].

In April 2020, the US CDC reported 1.7% of children under 18 years of age. with a diagnosis of COVID-19. In fact, the median age was 11 years and 57% were male; 2% of children were admitted to an ICU. It should be noted that children under 1 year of age represented the highest percentage of hospitalization (15 - 62%) [13].

In the first series published in China, only 0.9% of individuals with a diagnosis ofCOVID-19 were under 10 years of age and 1.2% were 10 to 19 years old 14. It has also been reported that, of the total number of infected children, 5.6% presented severe pathology (hypoxemia), and 0.6% of the total developed respiratory failure, multiple organ failure or acute respiratory distress syndrome (ARDS). Indeed, childrenarealsomorepronetocommunitytransmission, since they are usually asymptomatic carriers[15,16].

Despite the known data in adults and its expansion throughout the world, the epidemiological and clinical patterns of COVID-19 in the pediatric population still are unclear [5,17,18].

In the epidemiological surveillance of the pediatric population in China, it has been reported that COVID-19 has been detected more frequently in children with ARDS compared to metapneumovirus, but other more classical viral agents of the season, such as influenza, have not been evaluated. Many infectious diseases affect children differently compared to adults, so understanding these differences can provide significant information on the pathogenesis of the disease and the development of therapeutics [19].

Clinical signs

The clinical manifestations are based on the triad of fever, dry cough, and shortness of breath. In a series of patients younger than 18 years in the US, 73% had one or more symptoms of the clinical triad; fever (56%), cough (54%) and respiratory distress (13%). In

addition, other manifestations have been detailed such as: myalgias, odynophagia, headaches, rhinorrhea, nausea, vomiting, diarrhea, abdominal pain, anosmia, ageusia and various skin manifestations (urticarial, rash, ischemic or vasculitic). Likewise, it has been detailed Clinical syndromes associated with SARS-CoV-2 respiratory infection Table 1[20]. It should be noted that a lower prevalence of fever and rashes in adolescents compared to children and infants [21,22].

In the US, researchers have described that only 25.1% of the children studied had at least one typical COVID-19 symptom, such as fever, cough, and shortness of breath. On the other hand, 9.9% of infants manifested two characteristic symptoms. Indeed, 16.5% of the patients had respiratory symptoms such as cough and dyspnea; 13.9% presented gastrointestinal symptoms (nausea, vomiting, diarrhea, abdominal pain); 8.1% had dermatological symptoms (rashes); 4.8% had neurological symptoms (headaches), and 18.8% had other nonspecific symptoms, including fever, decay, myalgias, arthralgias, and smell or taste disorders. A frequency of hospitalization of 5.5% was described, among hospitalized patients 17.6% required admission to the ICU; in addition, 4.1% required mechanical ventilatory assistance.

By characterizing pediatric COVID-19 symptoms in the community and analyzing the association between symptoms and SARS-CoV-2 RNA levels, approximated by cycle threshold (Ct) values, in children and adults. In the community, SARS-CoV-2 RNA levels, as determined by Ct values, were reported to be significantly higher in symptomatic individuals than in asymptomatic individuals. But more research is needed to understand the role of SARS-CoV-2 RNA levels and viral transmission[24].

Table 1. Clinical syndromes associated with respiratory infection due to SARS-CoV-2

Infection no Complicated	Pa&#xfffd;ents with uncomplicated viral infec&#xfffd;on of the upper respiratory tract may present with nonspecific symptoms, such as fever, cough, sore throat, nasal conges&#xfffd;on, malaise, headache, muscle pain, or general malaise. There are no signs of dehydra&#xfffd;on, sepsis, or respiratory distress.
Mild infection of low routes1	Cough, respiratory distress + polypnea (in breaths / min): 92%. They may or may not have a fever.
Severe infection of low lanes	Cough or shortness of breath and at least one of the following: central cyanosis or SatO2 <60 mmHg, PaCO2> 50 mmHg. The diagnosis is clinical; chest images can exclude complica&#xfffd;ons (atelectasis, infiltrates, effusion).
Other demonstrations associated with grave pictures2	Coagula&#xfffd;on disorders (prolonged prothrombin &#xfffd;me and eleva&#xfffd;on of D-dimer), myocardial damage (increased myocardial enzymes, ST-T changes on the electro-cardiogram, cardiomegaly and heart failure), gastrointes&#xfffd;nal dysfunc&#xfffd;on, eleva-ted liver enzymes, and rhabdomyolysis.
Syndrome of distress acute respiratory (ARDS)	Onset: new or worse condi&#xfffd;on in the previous 10 days. Chest X-ray, CT or ECO: bilateral infiltrates, lobar or pulmonary atelectasis, or consolida&#xfffd;ons. Pulmonary edema: absence of other e&#xfffd;ology such as heart failure or volume overload. Oxygena&#xfffd;on (OI = Oxygena&#xfffd;on Index and OSI = Oxygena&#xfffd;on Index using SpO2): • Bilevel NIV or CPAP ≥5 cmH2O through a full face mask: PaO2 / FiO2 ≤ 300 mmHg or SpO2 / FiO2 ≤264 • Mild ARDS (ven&#xfffd;la&#xfffd;on invasive): 4 ≤ LE
Sepsis3	Suspected or proven infec&#xfffd;on and ≥ 2 criteria for SIRS, of which one must be an abnormal temperature or an abnormal white blood cell count.
Septic shock4	Any hypotension (SBP <5th percen&#xfffd;le or> 2 SD below normal for age) or 2-3 of the following: altered mental status; tachycardia or bradycardia (HR 160 bpm in infants and HR 150 bpm in children); slow capillary refill (> 2 seconds) or hot vasodila&#xfffd;on with preserved pulses; tachypnea; mo&#xfffd;led skin or petechial or purpuric rash; increased lactate, oliguria, hyperthermia or hypothermia.

1. Equivalent to WHO mild pneumonia. 2. Equivalent to severe WHO pneumonia. SIRS: Systemic inflammatory response syndrome. NIV: non-invasive ventilation, SBP: systolic blood pressure, SD: standard deviation. HR: heart rate. 3Goldstein B, Giroir B, Randolph A, International Consensus Conference on Pediatric Sepsis. International pediatric sepsis consensus conference: definitions for sepsis and organ dysfunction in pediatrics. Pediatric Crit Care Med 2005; 6: 2-8. 4 Davis AL, Carcillo JA, Aneja RK, et al. American College of Critical Care Medicine Clinical Practice Parameters for Hemodynamic Support of Pediatric and Neonatal Septic Shock. Crit Care Med 2017; 45: 1061-93.

***Source:** Spanish Society of Pediatrics, Clinical management document of the pediatric patient with SARS-CoV-2 infection, 2020.*

Laboratory diagnosis

After identifying a case as a suspect of COVID-19, the laboratory diagnosis is confirmed by taking a sample with the appropriate personal protective equipment.

Nucleic acid amplification tests

The real-time polymerase chain reaction (RT-PCR) test is considered the diagnostic standard for the detection of SARS-CoV-2 infection. In the case of a person who is exposed to an individual with a confirmed diagnosis, a window period of about five days has been observed between the exposure and the detection of nucleic acids in the test. For this reason, a pharyngeal exudate and a nasopharyngeal exudate sample will be sent, placed in a tube with viral transport medium. Bronchoalveolar lavage or tracheal aspirate in hospitalized individuals[25] are also considered useful samples.

Antigenic test for SARS-CoV-2

The rapid antigenic test for SARS-CoV-2 detects viral antigens and is carried out during the first seven days from the onset of symptoms, it is not indicated in asymptomatic people. Compared to RT-PCR it is less sensitive (detection of positive cases), but with similar specificity (detection of negative cases). It has the advantage that the results are immediate (15-30 min) [26].

Serology for SARS-CoV-2

Serological tests that detect antibodies to SARS-CoV-2 are also used to diagnose the disease and to measure response to vaccination. But the detection of antibodies does not always translate the existence of protective immunity, since not all antibodies produced in response to an infection are neutralizing. Generally speaking, IgM antibodies are detected in the first five days of infection and IgG-type antibodies are observed around 14 days after infection (they can appear even up to 21 days). In particular, these tests are not recommended alone for the diagnosis of SARS-CoV-2 infection [26-28].

Indeed, clinical, analytical and radiological alterations that can occur in acute viral respiratory disease in children are detailed [29].

Paraclinical parameters

According to published reports, in the majority of COVID-19 patients, the absolute value of lymphocytes was reduced. It appears that COVID-19 could induce a cytokine storm and activate immune responses that could appear as changes in the number of white blood cells and immune cells, especially lymphocytes. The clinical outcome of such events would trigger respiratory distress syndrome, septic shock, and eventually organ damage. COVID-19 may also present with hypoproteinemia, elevated aminotransferases, and a prolonged prothrombin time. Hepatotoxicity could be attributed to the increased expression of angiotensin II converting enzyme (ACE2) in cholangiocytes, ACE2 could act as an entry receptor for COVID-19[30].

It has been observed that a subset of patients with severe SARS-CoV-2 could develop “cytokine storm syndrome” (CRS), the clinical manifestations of which can range from mild flu-like symptoms to severe systemic inflammatory response syndrome (SIRS). Laboratory findings reflect the systemic inflammatory response, but abnormalities are highly variable and are influenced by the type or amount of activated cytokines. In general, the degree of elevation of cytokines and inflammation markers correlate with the severity of the clinical syndrome. In particular, the dramatic elevation of IL-6 is a supportive finding for the diagnosis of “cytokine storm syndrome” [31].

In a retrospective cohort study that included 191 patients with SARSCoV-2 from Wuhan, China, non-survivors, compared with survivors, presented more frequently with high LDH, elevated procalcitonin, increased levels of ferritin, and IL-6 elevated. Higher C-reactive protein (CRP) has been associated with unfavorable aspects of SARS-CoV-2 disease, such as the development of ARDS, higher levels of troponin-T, myocardial lesions, and death [31].

CRP is considered a nonspecific acute phase protein induced by IL-6 in the liver and a sensitive biomarker of inflammation, infection, and tissue damage. The level of PCR expression is usually low, but increases rapidly and significantly during acute inflammatory responses. Elevation of CRP alone or in combination with other markers can reveal bacterial or viral infections. The relationship between CRP and COVID-19 has been described, in fact, it was reported that patients with CRP> 41.8 mg / L were more likely to develop a serious disease [31].

In general, serum procalcitonin (PCT) levels are low or undetectable. PCT levels increase with bacterial infections and are relatively low with viral infections. Therefore, the validity of PCT as an independent factor to predict the severity of COVID-19 needs to be studied in depth.31. Furthermore, to describe the role of transferrin in the course of COVID-19, more extensive clinical-pathological investigations are still required[32].

Table 2. Possible clinical, analytical and radiological alterations in acute viral respiratory disease in children.

	Mild	Serious
Clinical picture	Fever (not always present), cough, nasal conges□on, runny nose, sputum, diarrhea, headache.	One week later, malaise, irritability, refusal to eat, hypoac□vity. In some cases, rapid progression (1-3 days), non-reversible respiratory failure with oxygen, sep□c shock, metabolic acidosis, coagulopathy, and bleeding.
Blood count	Normal leukocytes or mild leukopenia and lymphopenia.	Progressive lymphopenia. Neutrophil / lymphocyte ra□o: the higher the ra□o, the greater the risk of poor evolu□on.
C Reactive Protein	Normal	Normal or elevated (suspect bacterial superinfec□on).
Procalcitonin	Normal	PCT> 0.5 ng / mL (rule out bacterial superinfec□on).
Biochemistry	Normal	Elevated transaminases, LDH, muscle enzymes, myoglobin, D-dimer, ferri□n, hyperglycemia.
Chest x-ray	Normal or peripheral inters□□al infiltrates.	Bilateral ground glass opaci□es and mul□ple lung consolida□ons. Infrequent pleural effusion.
Chest CT	Ground glass images and infiltrates are more evident on CT than on radiography.	Mul□ple lobar consolida□ons may appear.

Source: Ministry of Health. Spain 2020. COVID-19 clinical management: hospital care.

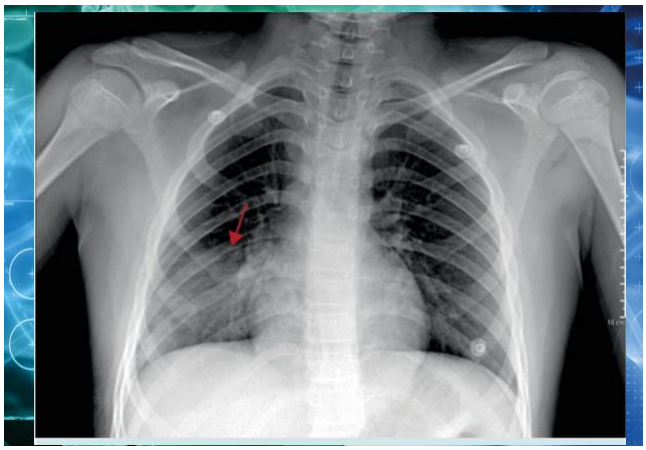
Diagnostic imaging

X-ray of chest

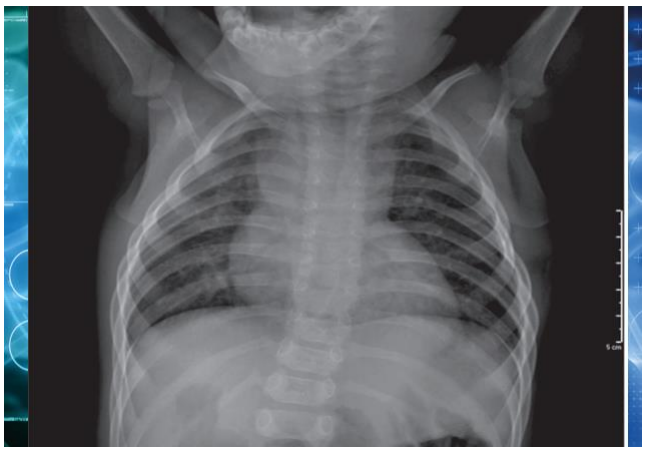
In laboratory-confirmed SARS-CoV-2 positive patients, a ground glass pattern and areas of consolidation predominantly in the lower and peripheral thirds have been evidenced (typical findings) (Figure 1.A). However, other atypical viral pneumonias can also show this pattern. The unilateral non-segmental or lobar ground glass pattern (Figure 1.B), consolidation or ground glass, and multifocalconsolidationwithnoparticulardistribution are more indeterminate findings. Peribronchial thickening with opacities is also included in this group of pediatric patients (Figure 1.C). On the other hand, various atypical findings are evident: unilateral segmental or lobar consolidation, centrally distributed parenchymal opacities, single rounded consolidation, with or without air bronchogram, pleural effusion and lymphadenopathy. According to the American College of Radiology, chest radiography in children is not indicated in patients younger than 3 months who do not require hospitalization. However, if the patient does not respond to outpatient treatment, requires hospitalization, or hospital-acquired pneumonia is suspected, the chest x-ray is considered a first step in the evaluation [33].

Figure 1. *Radiographic findings of the posteroanterior chest (PA)*

A. *A-17-year-old female patient, with a positive study for COVID-19 by TR PCR, with a chest x-ray in PA showing bilateral focal areas of radiodensity, predominantly peripheral and towards the lower lobes.*



B. *An 11-year-old male patient, with a positive study for COVID-19 by RT PCR, with a chest x-ray in PA, with a focal radiodensity area, with a faint ground-glass pattern, unique in the right lower lobe.*



C. *A 1-year-old male patient with a positive study for COVID-19 by RT PCR, with a chest radiographic film in PA, with a less typical finding consisting of an increase in the bronchovascular network, due to peribronchial thickening.*

Source: *De Uña-Flores A. Radiographic evaluation of the pediatric patient with COVID-19. Acta Pediatr Mex. 2020; 41 (Suppl: 1): 58-63.*

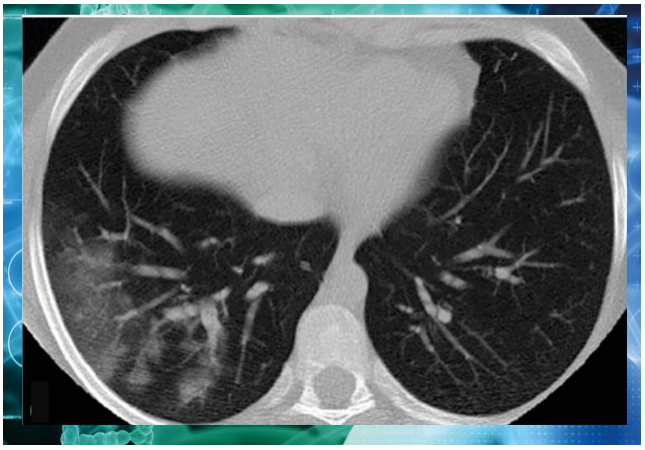
Chest computed tomography (CT) scan

Signs observed in chest CT have been described in an average time of onset between 1 to 15 days of illness. In fact, authors have calculated the average number of days with the different tomographic controls[34].

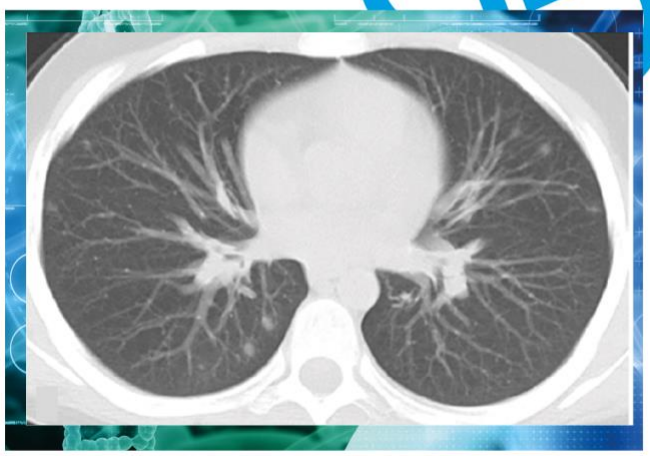
- *In the first 5 days, reticulum-nodular-granular images are detailed, especially in the periphery.*
- *In the next 5 days, multiple extensive radiodense images (lung with radiodense areas).*
- *From the 11th to the 14th, extended extension of Multiple extensive radiodense images with more heterogeneous appearance of spots, more condensing, with bronchograms, alveolar involvement predominates. In addition, the "HALO sign" is mentioned, which is interpreted as a condensing lesion surrounded by a heterogeneous interstitial border.*
- *4. In the case of good clinical evolution, a progressive decrease in lesions is identified[35].*

Figure 2. *Posteroanterior chest radiographic findings*

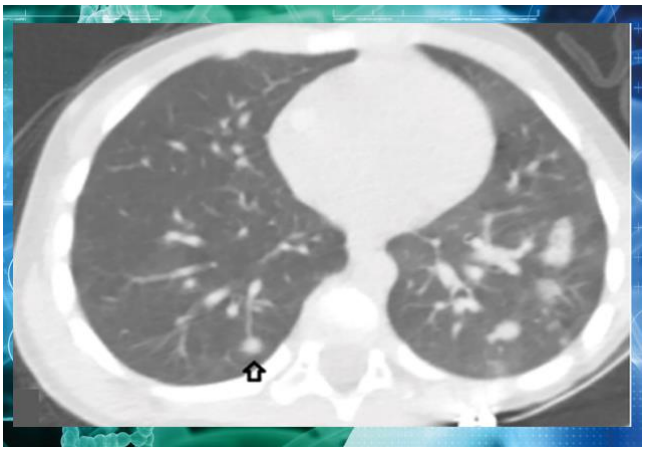
A. *The chest CT image in the axial plane revealed a unique peripheral ground-glass opacity in the poster basal segment of the right lower lobe. The opacity darkened with the right liver lobe and diaphragm on chest radiograph.*



B. *Imaging findings of a 10-year-old male patient with COVID-19. Chest computed axial tomography revealed ground-glass opacities of bronchovascular distribution in a 10-year-old male patient in the periphery of the basal segments of the right lower lobe.*



C. *Axial chest CT image of a 13-year-old male without contrast showing bilateral, multifocal, peripheral, and perivascularly distributed millimeter nodular ground glass opacities. The opacities were not detected on the chest radiograph due to the smaller size and lower density.*



D. *A chest computed tomography scan of a 3-year-old male patient was performed without contrast six days after the onset of fever and cough. The chest CT image shows round consolidations of bilateral, multifocal and perivascular distribution without halo sign. Note the signs on the feeding container (arrow).*

Source: *Zuhal Bayramoglu, MD, et al. Imaging Features of Pediatric COVID-19 on Chest Radiography and Chest CT: A Retrospective, Single-Center Study, 2020.*

Treatment

The main therapeutic strategies for the most compromised COVID-19 patient are based on continuous or periodic monitoring of vital signs, since sudden changes in the patient's condition have been described. In addition to oxygen to maintain saturation greater than or equal to 93%. It is considered that exaggerated volleysation can further affect respiratory and cardiovascular function[36].

In the presence of bronchial obstruction, due to the risk that nebulizations have of generating aerosols, it is suggested to use intramuscular epinephrine in doses similar to those of anaphylaxis. At this time, there is no scientific information to support the usefulness of lopinavir / ritonavir, azithromycin, or hydroxychloroquine in the treatment of SARS-CoV-2 infection. The indication and choice of antiviral treatment will be agreed, if possible, with the Infectology team. pediatric table 337. In case of further deterioration with respiratory failure or shock, the patient will require assisted ventilation. The strategy must be anticipatory, in such a way as to send early to an intensive care unit so that the decision of what type of ventilatory assistance will be indicated can be made under the best conditions.[37].

Table 3. Indications to assess specific treatment

Clinical picture	Chest X-ray / CT	Treatment	A□tude
MILD: no hypoxemia, no respiratory distress, or mild	Not indicated except risk groups.	Symptoma□c (1)	Home discharge except risk groups
	Finding of pneumonia	Specific treatment against SARS-CoV-2 (1)	Monitoring / home admission
MODERATE: hypoxemia and / or moderate respiratory distress	Normal	Symptoma□c (1)	Admission without an□viral treatment
	Any infiltrator	Specific treatment against SARS-CoV-2 (1)	Admission evalua□ng an□viral treatment
SEVERE (ICU, PICU): severe hypoxemia, severe respiratory distress, poor appearance	Any infiltrator	Specific treatment against SARS-CoV-2 (1)	Admission with combined an□viral treatment. Consider reques□ng compassionate use.

1: Empirical antibiotic therapy if bacterial coinfection or superinfection is suspected.

Source: *Ministry of Health. Spain 2020. COVID-19 clinical management: hospital care*

Corticosteroids

Its administration is not recommended for the treatment of viral pneumonia outside of clinical trials. In fact, in the initial phases (first week of symptoms), it could promote viral replication. The role of dexamethasone in children and the timing of its administration remain to be elucidated[37]. The WHO and CDC state that systemic glucocorticoids should not be used in patients with COVID-19, unless there are other indications such as exacerbation of chronic obstructive pulmonary disease[38-40].

Antibiotics:

they are not recommended except in suspected bacterial superinfection[29].

Hydroxychloroquine-chloroquine:

there is currently not enough evidence to indicate its use[39-40].

Lopinavir / ritonavir:

at the present time it is not indicated. Used in moderate-severe lung involvement alone or in combination with other drugs. It is not combined with other antivirals such as remdesivir [37,39].

Remdesivir:

is considered the only antiviral that has shown modest clinical benefit. It could be presented as a therapeutic option in pediatric patients with a severe or moderate infection associated with hypoxemia. The main adverse reaction is infusion hypotension [5,37,38,40,42].

Favipiravir:

Clinical trials for the treatment of COVID-19 are ongoing, but there is no evidence for pediatric patients[38.40].

Oseltamivir:

It is only considered in case of coinfection with influenza virus, since neuraminidase inhibitors do not act on COVID-19[40].

Anticoagulation:

Low molecular weight heparin (enoxaparin) prophylaxis could be considered individually in patients with risk factors for thrombosis[5-37].

Intravenous human immunoglobulin:

In addition to life support treatment, it is the predominant therapeutic option in different centers when Kawasaki disease is part of the differential diagnosis, associated with COVID-19[5]. They have been used in severe cases, but their indication and efficacy should be evaluated [37].

Tocilizumab:

the inhibition of IL-6 receptors promotes a reduction in cytokine production, thus configuring some indication of possible treatment for hyperinflammation, although there are no studies in the pediatric population [5,37,39].

Otocilizumab:

is approved by the United States Food and Drug Administration (FDA) for use in critical case cytokine release syndrome in adults and children, due to the similarity of cytokine release and cytokine storm in COVID-19[5].

IL-1 inhibitors:

Although there is no evidence of a correlation between serum IL-1 levels and COVID-19 severity, ongoing multicenter studies have evaluated the role of Inhibitors of IL-1 (anakinra) associated with emapalumab in reducing hyperinflammation in patients with severe SARS-CoV-2 infection[5].

TNF inhibitors (infliximab):

TNF is one of the triggers for the cytokine storm. Indeed, a meta-analysis with anti-TNF showed an improvement in survival in patients with sepsis, a situation in which the role of cytokines is also relevant, thus opening a therapeutic possibility in severe cases of COVID-19 [43].

Interferon-α2b:According to Chen's review in pediatric patients, interferon-α2b nebulization (100,000– 200,000 IU / kg for mild cases and 200,000 to 400,000 IU / kg for severe cases, twice daily for 5-7 days) could be applied prior multidisciplinary analysis[38].

Gammablobulin:

noevidencetorecommenditsuse.Ithasbeensuggested to use it in patients with hypogammaglobulinemia[39].

Plasma from convalescent patients:

a pilot study suggests that its administration is safe,

reduces viral load and may improve clinical outcomes. However, its use could only be administered as part of a compassionate treatment or within the framework of duly regulated clinical trials[38,40].

Conclusion

The progressive restart of face-to-face activities could increase the possibility of community transmission of SARS-CoV-2 among children. Although SARS-CoV-2 infection appears to have a mild course in most cases in pediatrics, severe cases that are not recognized and without prompt attention can lead to death. Therefore, it is critical to identify the clinical and epidemiological characteristics, as well as the clinical course in children with laboratory-confirmed COVID-19. It should be noted that specific antivirals against COVID-19 are not recommended, since there is no evidence to support a clinical benefit. The indication and choice of antiviral treatment will be agreed with the infectology teampediatric and The strategy must be anticipatory; it will be evaluated early and sent to an intensive care unit in cases that require it to avoid complications.

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1. González P, et al. COVID-19 in pediatrics: critical appraisal of the evidence. Annals of Pediatrics. Elsevier Doyma, 2021.

2. The COVID Project (Coronavirus in Kids Tracking and Education Project). Control panel of cases (incidence) COVID-19. 2020.

3. American Academy of Pediatrics and Children's Hospital Association. Children and COVID-19: State Data Report. 2020.

4. Liguoro I, Pilotto C, Bonanni M, Ferrari ME, Pusiol A, Nocerino A, et al. SARS-COV-2 infection in children and newborns: a systematic review. Eur J Pediatr. 2020 Jul; 179 (7): 1029-1046.

5. Simon Junior H, Sakano TMS, Rodrigues RM, Eisencraft AP, Carvalho VEL, Schvartsman C, Reis AGADC. Multisystem inflammatory syndrome associated with COVID-19 from the pediatric emergency physician's point of view. J Pediatr (Rio J). 2021 Mar-Apr; 97 (2): 140-159. doi: 10.1016 / j.jped.2020.08.004. Epub 2020 Sep 11. PMID: 32946801; PMCID: PMC7486073.

6. Broad J, Forman J, Brighouse J, Sobande A, et al. PIMS-TS study group. Post-COVID-19 pediatric inflammatory multisystem syndrome: association of ethnicity, key worker and socioeconomic status with risk and severity. Arch Dis Child. 2021 Mar 16: archdischild-2020-320388.

7. Romero C. 12. Risk factors in SARS-CoV-2 (COVID-19) disease. Scientific reports COVID-19: 100.

8. Burki T. COVID-19 in Latin America. Lancet Infect Dis. 2020 May; 20 (5): 547-548.

9. CDC COVID-19 Response Team. Coronavirus Disease 2019 in Children - United States, February 12-April 2, 2020. MMWR Morb Mortal Wkly Rep. 2020 Apr 10; 69 (14): 422-426.

10. Livingston E, Bucher K. Coronavirus Disease 2019 (COVID-19) in Italy. JAMA. 2020 Mar 17.

11. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) Outbreak in China: Summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. JAMA. 2020.

12. Olmos C, Cepeda J, Zenteno D. New coronavirus (COVID-19) in the general and pediatric population: An epidemiological review. Chile 2020. Neumol Pediatr. 2020; 15 (2): 293-300.

13. Santana-Caicedo A. Multisystemic inflammatory syndrome and COVID-19 in children: Risk of Morbidity and Mortality. Knowledge Pole 6.7 (2021): 240-254.

14. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. JAMA. 2020; 323: 1239-42.

15. Sinha I, Harwood R, Semple M, Hawcutt D, Thursfield B, Narayan O, et al. COVID-19 infection in children. Lancet Respir Med. 2020. doi: 10.1016 / S2213-2600 (20) 30152-1.

16. Dong Y, Mo X, Hu Y, Qi X, Jiang F, MD, Jiang Z, et al. Epidemiology of COVID-19 among children in China. Pediatrics. 2020; 145: e20200702.

17. Gutiérrez-Hernández O. Do weather and climate influence the distribution of the new coronavirus (SARS CoV-2)? A review from a biogeographic perspective. (2020).

18. Dong Y, Mo X, Hu Y, Qi X, Jiang F, Jiang, et al. Epidemiology of COVID-19 Among Children in China. Pediatrics. 2020; 145 (6): p. DOI: 10.1542 / peds.2020-0702.

19. Ferreira C, et al. COVID-19 epidemiology in pediatrics. Ferreira. 2020 ;: p. 23-24.

20. Spanish Society of Pediatrics. Document on the clinical management of a pediatric patient with SARS-CoV-2 infection. AEP. 2020; p. 5.

21. Castagnoli R, Votto M, Licari A, Brambilla I, Bruno R, Perlini S, et al. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection in children and adolescents. A systematic review. JAMA Pediatr. doi: 10.1001 / jamapediatrics.2020.1467.

22. Recalcati S. Cutaneous manifestations in COVID-19: a first perspective. J Eur Acad Dermatol Venereol. 2020. doi: 10.1111 / jdv.16387.

23. Patch V, Booker KS, Kalra R, et al. A retrospective cohort study of 12,306 pediatric COVID-19 patients in the United States. Sci Rep. 2021 May 13; 11 (1): 10231. doi: 10.1038 / s41598-021-89553-1. PMID: 33986390; PMCID: PMC811969.

24. Chung E, Chow E, Wilcox N, Burstein R, et al. Comparison of Symptoms and RNA Levels in children and adults with SARS-CoV-2 Infection in the Community Setting. JAMA Pediatr. 2021 Jun 11.

25. General Directorate of Epidemiology. Standardized guideline for epidemiological and laboratory surveillance of viral respiratory disease, Mexico December 2020.

26. COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. National Institutes of Health. Available at https:// www.covid19treatmentguidelines.nih.gov/.

27. Sethuraman N, Jeremiah SS, Ryo A. Interpreting diagnostic tests for SARS-CoV-2. JAMA. 2020; 323 (22): 2249-2251.

28. Guo L, Ren L, Yang S, et al. Early humoral response to diagnose novel coronavirus disease (COVID-19). Clin Infect Dis. 2020; 71 (15): 778-785.

29. Ministry of Health. Spain. COVID-19 clinical management: hospital care. 2020.

30. Mohammadi-Samani, Parisa Ghasemiyeh and Soliman. COVID-19 outbreak: Challenges in pharmacotherapy based on pharmacokinetic and pharmacodynamic aspects of drug therapy in patients with moderate to severe infection. Heart & Lung. 2020 ;: p. 764.

31. MSP. Consensus of hematology recommendations on the treatment of COVID-19. MTT2- NATIONAL. 2020; p. 20-23.

32. Mesa-González M, et al. Potentialities of transferrin as a prognostic biomarker of COVID-19. SARS - COV - 2 Medical Update. 2020; p. 18.

33. De Uña-Flores A. Radiographic evaluation of the pediatric patient with COVID-1f. Acta Pediátrica México. 2020; p. S60.

34. Gentilea L, et al. COVID-19. Radiological images. Buenos Aires Children's Hospital Magazine. 2020; p. 146.

35. Bayramoglu Z, Canıpek E, Comert RG, Gasimli N, Kaba O, Sarı Yanartaş M, Hançerli Torun S, Somer A, Erturk SM. Imaging features of pediatric COVID-19 on Chest radiography and chest CT: A Retrospective, Single-Center Study. Acad Radiol. 2021 Jan; 28 (1): 18-27. doi: 10.1016 / j.acra.2020.10.002. Epub 2020 Oct 5. PMID: 33067091; PMCID: PMC7534757.

36. Whittle J, Pavlov I, Sacchetti A, Atwood C, Rosenberg M. Respiratory support for adult patients with COVID-19. JACEP Open. 2020; 1-7.

37. Spanish Society of Pediatrics. Document on the clinical management of a pediatric patient with SARS-CoV-2 infection. Extract from the Clinical Management Document of the Ministry of Health. 2020.

38. Tezer H, Bedir Demirdağ T. Novel coronavirus disease (COVID-19) in children. Turk J Med Sci. 2020 Apr 21; 50 (SI-1): 592-603. doi: 10.3906 / sag-2004-174. PMID: 32304191; PMCID: PMC7195991.

39. Perillán J, et al. Treatment of SARS-CoV-2 infection in pediatrics. Chile's Pediatric Guide. 2020; p. 353.

40. Taffarelay P, Jorro F. The critical pediatric patient with COVID-19. Argentine Pediatric Guide. 2020; p. e460.