Residência RP Pediátrica
Publicação Oficial da Sociedade Brasileira de Pediatria
ISSN-Online: 2236-6814

Submitted on: 08/15/2020
Approved on: 09/11/2020

ORIGINAL ARTICLE

# Proposal of systematic approach of COVID-19 in pediatric population

Andrea Maciel de Oliveira Rossoni[1], Tatiane Hirose[1], Adriana Koliski[1], Marcelo Rodrigues[1], Valéria Cabral Neves[1], Lucciano Massuda[1], Tony Tannous Tahan[1], Débora Carla Chong-Silva[1]

**Keywords:**
Severe Acute Respiratory Syndrome, Treatment Outcome, Coronavirus Infections, Child.

## Abstract

**Introduction:** Developing an approach protocol for COVID-19 in pediatrics is a great challenge, since the current recommendations are much more based on the reality evidenced by cases in adults. However, a protocol that assists in the management of suspected and confirmed cases in pediatric units can be useful, despite the fact that most severe respiratory cases in children have other viruses as their main etiology. **Objectives:** To suggest a systematic and practical approach to children in the new coronavirus pandemic. **Results:** Systematize, from the organization of the space for assistance, team IPE use, clinical classification, etiological, and laboratory investigation, categorization of suspected cases to the pharmacological approach. **Conclusions:** In the face of so many uncertainties, it is essential to organize pediatric care and mitigate risks, mistakes and anxieties during this pandemic.

[1] Hospital de Clínicas - Federal University of Paraná, Pediatrics Department - Curitiba - Paraná - Brazil.

**Correspondence to:**
Débora Carla Chong-Silva.
Complexo Hospital de Clínicas UFPR. Rua Gen. Carneiro, 181, Alto da Glória, Curitiba, PR Brazil. CEP: 80060-900. E-mail: debchong@uol.com.br


DOI: 10.25060/residpediatr-2021.v11n1-441

This work is licensed under a Creative Commons Attribution 4.0 International License.

## INTRODUCTION

The World Health Organization declared COVID-19 a pandemic on March 11, 2020[1,2].

The novel coronavirus named SARS-CoV-2 is an RNA virus of the *Coronavirinae* subfamily that causes the disease known as COVID-19[1-3].

For reasons still under investigation, children develop milder disease, although they play an important role in the community spread of the virus[1-3].

Designing a pediatric care protocol for COVID-19 is challenging, since current recommendations are based on evidence derived from cases of the disease in adults. Nevertheless, a protocol to assist the management of suspected and confirmed cases of the disease may be useful, although other viruses – such as the respiratory syncytial virus – cause the majority of the cases of severe respiratory involvement in children.

The proposed systemic approach ranges from the organization of the workspace where patients are seen, the personal protective equipment (PPE) worn by care team members, the categorization of clinical findings and suspected cases, the investigation of the etiology of the disease and lab workup findings, to the prescription of drug therapy when needed, with the purpose of aiding pediatricians and physicians from other medical specialties through this critical moment.

### The proposed systematic approach includes the following

1) TRIAGE
2) WEARING PPE
3) CLINICAL EVALUATION and RISK ASSESSMENT
4) THERAPEUTIC APPROACH
5) CATEGORIZATION OF CASES (COVID-19 Probability Scores) and TESTING

## 1. TRIAGE

Quick triage starts when patients and their companions arrive at the health clinic and is performed by a team equipped with proper PPE so that subjects with acute respiratory symptoms (suspected for COVID-19) are segregated from asymptomatic individuals. Pediatric patients and their companions must be asked about the presence of the following symptoms: coughing, fever, coryza, myalgia, sore throat, dyspnea, diarrhea, and whether they were in contact with individuals suspected for or diagnosed with COVID-19 within the last 14 days. If the patient and/or their companion says yes to one or more questions, they must be sent, after sanitizing their hands with 70% alcohol and putting surgical masks on, to the place in the Pediatric Emergency Unit designated for suspected cases (isolated rooms with care teams equipped with PPE)[1-3].

**SUSPECTED CASES**

- Children with respiratory symptoms, with or without fever or baseline disease (asthma included), or without respiratory symptoms but with a symptomatic companion;
- Children with other, non-respiratory symptoms such as gastrointestinal symptoms must be assessed case by case.

## 2. WEARING PPE

When seeing patients suspected for COVID-19, care team members must wear the PPE specified in the standards defined by the Hospital Infection Control Committee, which include: disposable cap, apron, surgical mask (in aerosol-generating procedures, N95 or PFF-2 masks are required), goggles or face shield, and disposable gloves[4].

**REQUIRED PPE FOR CARE TEAM MEMBERS**

- Cap, Apron, Mask, Goggles or face shield, Gloves
  - In aerosol-generating procedures, **N95 or PFF-2** masks are required

## 3. CLINICAL EVALUATION and RISK ASSESSMENT

After triage, patients are assessed by the assisting team at the emergency department and categorized based on severity of involvement[1-3,5].

**SIGNS OF SEVERE INVOLVEMENT**

- Tachypnea or respiratory distress and/or
- Saturation < 95% in ambient air and/or
- Fever for more than three days and/or
- Prostration, signs of toxemia, shock or sepsis and/or
- Deterioration of clinical manifestations of preexisting disease.

**HIGH RISK PATIENTS**

- Infants aged less than one year or
- Subjects with **comorbidities**

**MILD INVOLVEMENT**

- Unspecific symptoms: fever, fatigue, coughing, anorexia, malaise, muscle pain, sore throat, congested nose or headache;
- Fever may not occur and gastrointestinal symptoms may be present;

**MODERATE INVOLVEMENT**

- Pneumonia **without complications or warning signs;**
- More frequent fever, coughing or difficulty breathing and tachypnea, **still without hypoxemia;**
- Some patients may not present signs or symptoms of severe involvement, although they have **altered CT scans** with subclinical lung injury.

**SEVERE INVOLVEMENT**

- Pneumonia with **dyspnea** and/or
- **Central cyanosis, saturation < 95%, signs of respiratory distress and/or**
- Systemic warning signs: difficulty sucking or drinking, lethargy or unconsciousness or seizures.

**CRITICAL INVOLVEMENT**

- Severe acute respiratory syndrome (SARS) and/or
- Shock and/or
- Encephalopathy and/or
- Myocardial injury and heart failure and/or
- Coagulation disorders and/or
- Acute kidney injury.

## 4. THERAPEUTIC APPROACH

Therapy must be initiated based on the severity assigned to each case. Patients categorized as having mild involvement must be offered treatment at home[6-13].

| Respiratory symptoms **without** severe involvement or underlying disease | Respiratory symptoms **with** warning signs | SARS<br>Sepsis with or without organ dysfunction |
|---|---|---|
| Treatment at home | Treatment at Pediatric Ward | ICU hospitalization |
| • No need for lab workup<br>• Consider chest X-rays, CBC, and biochemical tests for patients with comorbidities<br>• Antipyretics; avoid anti-inflammatory agents<br>• Oseltamivir (in cases of influenza-like illness)<br>• Consider amoxicillin in patients suspected for bacterial infection<br>• Assess the need to prescribe corticosteroids and bronchodilators; keep continuous use medication<br>• Isolation at home for the whole family for 14 days (from symptom onset)<br>• **Advise patients about signs of severe involvement requiring care at a clinic:** worsening or persistent fever, signs of respiratory distress, worsening general condition. | • Ventilatory support when needed (non-rebreather mask or nasal cannula, maximum of 3l/min): to maintain saturation ≥ 95%<br>• Hemodynamic support<br>• Oseltamivir (in cases of influenza-like illness)<br>• Consider ampicillin if the patient is suspected for bacterial infection<br>• Assess the need for corticosteroids and bronchodilators<br>• Viral diagnosis (RT-PCR) and blood culture<br>• Monitor hemodynamic status and workup results<br>• Manage imaging and workup findings as needed<br>• Check for **signs of severe involvement:** deterioration of clinical signs and organ dysfunction | • Ventilatory support ($O_2$ Venturi mask/nebulizer, high-flow nasal cannula, NIV or OTI) – aerosol reduction protocol<br>• Hemodynamic support<br>• Oseltamivir (in cases of influenza-like illness)<br>• Consider ceftriaxone + oxacillin if the patient is suspected for bacterial infection<br>• Assess the need for steroids and bronchodilators<br>• Viral diagnosis (RT-PCR) and blood culture<br>• Monitor hemodynamic status and workup results<br>• Manage imaging and workup findings as needed |

Restricted use of nebulizers.
If required, **advise assisting team to wear PPE against aerosols** (N95 or PFF-2 mask)

While measuring saturation levels, take measurements with the oximeter for at least one minute from more than one limb.

Key: CBC= complete blood count, NIV= non-invasive ventilation, OTI= orotracheal intubation, RT-PCR= reverse transcription-polymerase chain reaction

**TESTING REQUIREMENTS**

- **Mild involvement:**
  - No testing needed. In patients with comorbidities, consider chest X-rays, CBC, and or biochemical tests.
- **Moderate to critical involvement:**
  - CBC, C-reactive protein, blood culture, viral diagnostic tests (SARS-CoV-2 and other viruses), arterial blood gas, blood urea nitrogen, creatinine, electrolyte levels.
- Severe cases:
  - GOT/GPT, aPTT, LDH, ferritin, CK, CK-MB, D-dimer, and troponin
- Chest X-rays for patients suspected for pneumonia
- Chest CT scans in cases of deterioration of clinical signs or signs of complication

**Antibiotics**
- Ampicillin: 200mg/kg/d, 6/6h, for 7 d
- Ceftriaxone: 80mg/kg/d, 24/24h, for 7 d
- Oxacillin: 200mg/kg/d, 6/6h, for 7 d

If prescribing **azithromycin** is deemed beneficial (anti-inflammatory, antiviral, or antibiotic properties)
Azithromycin: 10 mg/kg, 1x/d, for 5-10 days

**Antivirals**
- Oseltamivir (12/12h, for 5 d):

Ages < 1 year:
< 3 months: 12 mg dose;
3 – 5 months: 20 mg;
6 – 11 months: 25 mg;

Ages ≥ 1 year:
< 15kg: 30 mg;
15 to 23 kg: 45 mg;
23 to 40 kg: 60 mg;
≥ 40 kg: 75 mg

**Chart 1.** Guidance on the intubation of patients suspected for COVID-19[7]:

**TESTING REQUIREMENTS**

- **Mild involvement:**
  - No testing needed. In patients with comorbidities, consider chest X-rays, CBC, and or biochemical tests.
- **Moderate to critical involvement:**
  - CBC, C-reactive protein, blood culture, viral diagnostic tests (SARS-CoV-2 and other viruses), arterial blood gas, blood urea nitrogen, creatinine, electrolyte levels.
- Severe cases:
  - GOT/GPT, aPTT, LDH, ferritin, CK, CK-MB, D-dimer, and troponin
- Chest X-rays for patients suspected for pneumonia
- Chest CT scans in cases of deterioration of clinical signs or signs of complication

**Antibiotics**
- Ampicillin: 200mg/kg/d, 6/6h, for 7 d
- Ceftriaxone: 80mg/kg/d, 24/24h, for 7 d
- Oxacillin: 200mg/kg/d, 6/6h, for 7 d

If prescribing **azithromycin** is deemed beneficial (anti-inflammatory, antiviral, or antibiotic properties)
Azithromycin: 10 mg/kg, 1x/d, for 5-10 days

**Antivirals**
- Oseltamivir (12/12h, for 5 d):

Ages < 1 year:
< 3 months: 12 mg dose;
3 – 5 months: 20 mg;
6 – 11 months: 25 mg;

Ages ≥ 1 year:
< 15kg: 30 mg;
15 to 23 kg: 45 mg;
23 to 40 kg: 60 mg;
≥ 40 kg: 75 mg

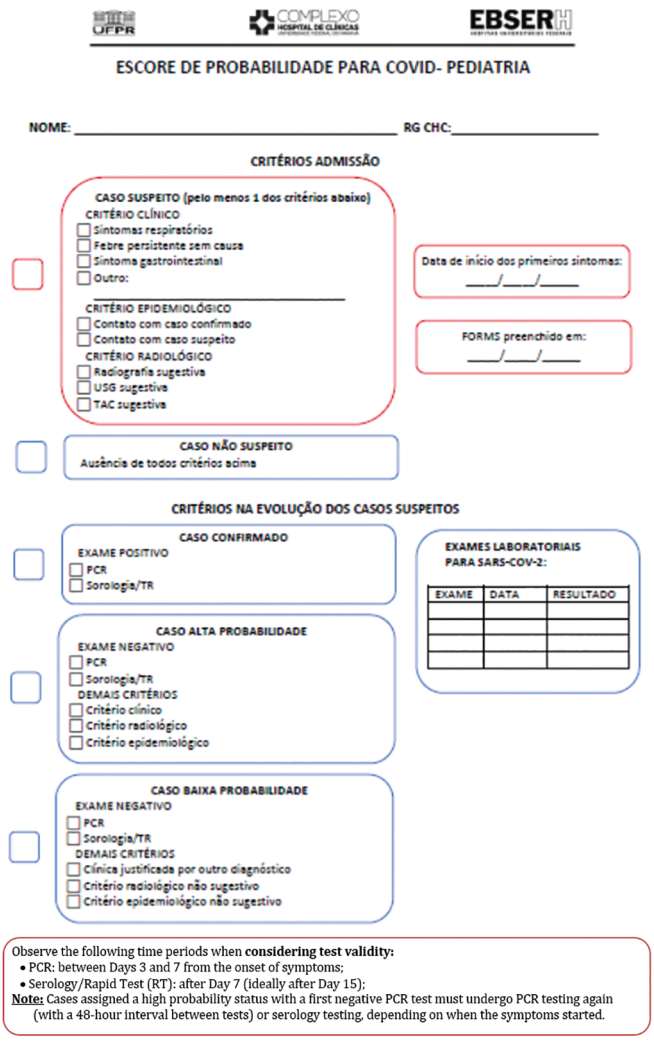
**Chart 2.** Physiotherapy and aerosol-generating procedures.

- **High risk procedures:** suction and collection of upper airway secretions; assisting in tracheal intubation and elective tracheal extubation; changing barrier filters, breathing circuits, and closed suction systems; handling and positioning patients.
- Nebulizers and oxygen therapy devices must be handled by care team members wearing the required PPE, in isolated rooms and preferably under negative pressure.
- Keep cuff pressure between 25 and 30 $cmH_2O$, so as to avoid leaks.
- Use of a closed suction system is recommended.
- Calculate the oxygenation index (OI) using the formula (OI= MAP x FiO2 x 100/ $PaO_2$) to assess ARDS severity in pediatric patients.
  - Mild ARDS (4< IO <8)
  - Moderate ARDS (8<IO<16)
  - Severe ARDS (IO>16)
- Monitor and keep driving pressure levels ≤ 15 $cmH_2O$ with a plateau pressure limit set at 28 $cmH_2O$.

Key to Boxes 4.1 and 4.2: CK= creatinine kinase, CK-MB= creatinine kinase MB fraction, $FiO_2$= fraction of inspired oxygen ($FiO_2$), HME= Heat and moisture exchanger, HEPA= High Efficiency Particulate Arrestance, LDH= lactate dehydrogenase, MAP= mean airway pressure, $PaO_2$= oxygen arterial pressure, ARDS= acute respiratory distress syndrome, aPTT= activated partial thromboplastin time, GOT= glutamic oxaloacetic transaminase, GPT= glutamic pyruvic transaminase.

## 5. CATEGORIZATION OF CASES (COVID-19 Probability Scores) and TESTING

Patients meeting the criteria for hospitalization may be referred to different care options and monitored during their stay. The categories to which patients were assigned at admission must be confirmed throughout hospitalization with testing (RT- PCR, Serology, or rapid diagnostic tests)[1-3,6].




## 6. RELEVANT CONSIDERATIONS

- The decision to prescribe **antibiotics** must be individualized, particularly when the patient is suspected for an associated bacterial infection[6-13].
- Empirical use of **oseltamivir** is indicated in cases suspected for **influenza-like illness / SARS**, regardless of severity of involvement, until the patient has a positive PCR test for coronavirus infection; the drug should be maintained of the patient tests positive for influenza[6-13].
- **Systemic corticosteroids** must be administered with caution and only in exceptional cases. Lack of evidence of efficacy of this drug class against COVID-19 and potential harm (delayed viral clearance) suggest that corticosteroids should be avoided and used only if other clinical circumstances acquire greater relevance, including asthma exacerbation, COPD, or septic shock. Corticosteroids may be administered to subjects with COVID-19 in cases of rapid, progressive deterioration of lung injury,

encephalitis or encephalopathy, hemophagocytic syndrome, or other severe complications[6-17].

- In June 16, 2020, Oxford University published the preliminary results of the Recovery (***R**andomized **E**valuation of **COV**id-19 th**ER**ap**Y)*** trial, a randomized controlled trial, which showed that 6 mg of oral or intravenous dexamethasone 1x/day for 10 days decreased the mortality of patients on mechanical ventilators or oxygen therapy (since then its use has been indicated by the Brazilian Society of Infectious Diseases). In a warning notice, the Brazilian Society of Pediatrics stressed the fact that patients in the pediatric age range are still being recruited to test the efficacy of dexamethasone in this population, and that the results observed in adults should not be extrapolated to children. The Society also advised over the consequences to one's health stemming from the use and overuse of corticosteroids without medical recommendation (fluid and electrolyte disorders, musculoskeletal and gastrointestinal alterations, skin reactions, psychiatric disorders, damage to the endocrine, ophthalmic, metabolic, immune, hematologic, and cardiovascular systems)[6,7,13-17].
- Children with asthma should not discontinue maintenance therapy (inhaled corticosteroids, long acting bronchodilators, immunobiologicals, or immunotherapy)[5].
- There is no scientific evidence to support the indication of **specific therapies for children with COVID-19.** Proposed therapies must have been tested in controlled trials and treatment should only be administered with the consent of the child's parents or guardians, whether they include antivirals (remdesivir, lopinavir/ritonavir) or adjuvant therapies (IL-6 inhibitors, interferon beta-1b, convalescent plasma therapy)[6,7,12-17].
- In previous studies, **azithromycin** was effective against the Zika and Ebola viruses *in vitro*, in addition to preventing severe airway infection when prescribed to patients with viral infection. Prescribing azithromycin to patients with COVID-19 might be justified based on a number of assumptions: the drug's antiviral, anti-inflammatory (potentially useful in the acute and chronic stages of the disease), and antibacterial (patients with COVID-19 often present with bacterial coinfection) effects, not to mention the good safety profile of the medication in adults and children. A number of studies currently in progress (93 in June 26 on https://www.clinicaltrials.gov) should soon shed light on the use of azithromycin alone or in association with other drugs and its effectiveness against COVID-19, particularly in children[7-11].
- The use of **nebulizers** should be discouraged on account of the risk of spreading aerosols. When needed in a hospital setting (patients with croup or cystic fibrosis), care teams must wear PPE with protection against aerosols (N95 or PFF-2 masks). The use of nebulizers in maintenance therapy (corticosteroids, antibiotics, etc.) for children without exacerbation staying at home should not be discontinued[5].
- No studies have looked into the use of **anticoagulation therapy** in children with COVID-19. Retrospective studies enrolling adult patients with COVID-19 have described cases of disseminated intravascular coagulation with altered D-dimer levels, suggesting that anticoagulant therapy might improve the outcomes of severely ill patients, particularly subjects with significantly elevated D-dimer levels. The decision to offer anticoagulant therapy to critically ill children diagnosed with coronavirus infection must be made with caution, considering the circumstances of each individual patient and with the input of the assisting care team[18].
- Adherence to the **immunization schedule** is recommended by the Brazilian Society of Pediatrics and the Brazilian Society for Immunization, along with measures and adjustments needed to safeguard patients and care team members to prevent the dissemination of vaccine-preventable diseases[5,13].

Despite the challenges introduced by frequent changes in scientific literature, particularly in regard to drug therapies, and the scarcity of studies involving children and adolescents, it is imperative to develop protocols for the pediatric population.

## ACKNOWLEDGEMENTS

I would like to thank the Heads of the Pediatrics Unit at the Hospital de Clínicas of the Federal University of Paraná; *Nurses Maria Gabriela Mendes Pereira, Mayara Caroline Barbieri, and Laressa Manfio Monteiro; Eduardo Kaehler Meister, MD;* the Head of the Pediatric Intensive Care Unit, *Prof. Dr. José Eduardo Carreiro;* the Head of the Pediatrics Department of the Federal University of Paraná, *Prof. Dr. Rubens Cat*; and pediatric pulmonologist *Prof. Dr. Carlos Antônio Riedi*, for their invaluable contributions and support in the development of a protocol to meet the needs of children in the pandemic.

## REFERENCES

1. Dong Y, Mo X, Hu Y, Qi X, Jiang F, Jiang Z, et al. Epidemiological characteristics of 2143 pediatric patients with 2019 coronavirus disease in China. Pediatrics. 2020 Jun;145(6):e20200702.
2. Shi Y, Tan M, Chen X, Liu Y, Huang J, Ou J, et al. Immunopathological characteristics of coronavirus disease 2019 cases in Guangzhou, China. Immunology. 2020 Mai;160(3):261-8. DOI: https://doi.org/10.1101/2020.03.12.20034736.

3. ZhengF, LiaoC, FanQH, ChenHB, ZhaoXG, XieZG,et al.Clinical characteristics of children with coronavirus disease 2019 in Hubei, China. Curr Med Sci. 2020 Mar;40:275-80. DOI: https://doi.org/10.1007/s11596-020-2172-6.
4. She J, Liu L, Liu W. COVID-19 epidemic: disease characteristics in children. J Med Virol. 2020 Jul;92(7):747-54.
5. Sociedade Brasileira de Pediatria (SBP). Orientações aos pacientes e cuidadores de crianças com asma na pandemia de COVID-19 [Internet]. Rio de Janeiro: SBP; 2020; [acesso em 2020 Jun 08]. Disponível em: https://www.sbp.com.br/fileadmin/user_upload/DC_Alergia_-_Covid-19.pdf
6. Italian Thoracic Society (ITS). Associazone Italiana Pneumologi Ospedalieri (AIPO). Italian Respiratory Society (SIP). Managing the respiratory care of patients with COVID-19 [Internet]. Milão: ITS/AIPO/SIP; 2020; [acesso em 2020 Jun 10]. Disponível em: http://www.sipirs.it/cms/wp-content/uploads/2020/03/Managing-the-Respiratory-care-of-patients-with-COVID-19.pdf
7. World Health Organization (WHO). COVID-19 clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected. Interim guidance 13 March 2020 [Internet]. Geneva: WHO; 2020; [acesso em 2020 Jun 08]. Disponível em: https://apps.who.int/ iris/handle/10665/33144
8. GautretP, LagierJC, ParolaP, HoangVT, MeddebL, MailheM,et al. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. Int J Antimicrob Agents. 2020 Jul;56(1):e105949. DOI: https://doi.org/10.1016/j.ijantimicag.2020.105949
9. Bacharier LB, Guilbert TW, Mauger DT, Boehmer S, Beigelman A, Fitzpa- trick AM, et al. Early administration of azithromycin and prevention of severe lower respiratory tract illnesses in preschool children with a history of such illnesses: a randomized clinical trial. JAMA. 2015 Nov;314(19):2034-44.
10. Damle B, Vourvahis M, Wang E, Leaney J, Corrigan B. Clinical pharmacology perspectives on the antiviral activity of azithromycin and use in COVID-19. Clin Pharmacol Ther. 2020 Abr;108(2):201-11. DOI: https://doi.org/10.1002/cpt.1857
11. Site https://www.clinicaltrials.gov [acesso em 2021 AGO 04), pesquisa Covid19 x Azithromycin, resultado em https://clinicaltrials.gov/ct2/results?cond=Covid19&term=azithromycin&cntry=&state=&city=&dist=
12. Zhang L, Peres T, Silva MVF, Camargos P. What we know so far about coronavirus disease 2019 in children: a meta-analysis of 551 laboratory-confirmed cases. Pediatr Pulmonol. 2020 Jun;55(8):2115-27.
13. Sociedade Brasileira de Pediatria (SBP). COVID-19 em crianças: envolvimento respiratório [Internet]. Rio de Janeiro: SBP; 2020; [acesso em 2020 Jun 16]. Disponível em: https://www.sbp.com.br/imprensa/detalhe/nid/covid-19-em-criancas-envolvimento-respiratorio/
14. Sociedade Brasileira de Pediatria (SBP). Síndrome inflamatória multissistêmica em crianças e adolescentes provavelmente associada à COVID-19: uma apresentação aguda, grave e potencialmente fatal [Internet]. Rio de Janeiro: SBP; 2020; [acesso em 2020 Jun 10]. Disponível em: https:// www.sbp.com.br/imprensa/detalhe/nid/sindrome-inflamatoria--multissis- temica-em-criancas-e-adolescentes-provavelmente-associada--a-covid-19- -uma-apresentacao-aguda-grave-e-potencialmente-fatal/
15. Wang, Y, Zhu F, Wang C, Wu J, Liu J, Che X, et al. Children hospitalized with severe COVID-19 in Wuhan. Pediatr Infect Dis J. 2020 Jul;39(7):e91-e4.
16. Shen K, Yang Y, Wang T, Zhao D, Jiang Y, Jin R, et al. Diagnosis, treatment, and prevention of 2019 novel coronavirus infection in children: experts' consensus statement. World J Pediatr. 2020 Jun;16(3):223-31.
17. Sociedade Brasileira de Pediatria (SBP). Comunicado aos Pediatras! Uso de dexametasona no tratamento da COVID-19. Posicionamento dos departamentos científicos de alergia, endocrinologia e pneumologia – SBP [Internet]. Rio de Janeiro: SBP; 2020; [acesso em 2020 Jun 16]. Disponível em: https://www.sbp.com.br/fileadmin/user_upload/22602b--NA_-_Uso_de_dexametasona_tratamento_COVID19.pdf
18. Ferranti JF, Rodriguez IS, Motta E, Johnston C, Carvalho WBB, Delgado AF. Beyond ventilatory support: challenges in general practice and in the treatment of critically Ill children and adolescents with SARS-CoV-2 infection. Rev Assoc Med Bras. 2020 Abr;66(4):521-7.