

Latin American Consensus of Clinical Management of Pediatric Patients with COVID-19 in the Pediatric Emergency Department: Latin American Society of Pediatric Intensive Care (SLACIP) Emergency Committee

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Abstract

During the last few months, a new type of virus from the Coronaviridae family was identified as a causative agent of severe pneumonia and a high number of infections in a short time period. It has been named as COVID-19 (SARS-CoV-2).

In a very short time, a large number of cases presented worldwide with high mortality in certain conditions and specific groups. Even though it presents at different degrees of severity, it mainly affects adults, the pediatric population is particularly exposed and participates in the spreading process; therefore, the efforts in this population are mainly focused on prevention, especially in risk conditions; identification and management strategies for positive cases for which there is still no evidence-based treatment available.

The main purpose of this publication is to present the recommendations of a general management protocol stated by the Emergency Committee of SLACIP (Latin American society of pediatric intensive care) due to the increase of cases in the context of a multinational collaborative work between our pediatric emergency departments and adjusted to each reality and criteria of clinical management.

These recommendations may vary as our knowledge and experience do; the epidemiological and economic situation in each country must be considered in the decision-making process.

Keywords: COVID-19 (SARS-CoV-2); SLACIP (Latin American Society of Pediatric Intensive Care)

Introduction

The first case of coronavirus in Latin America was reported on February 26, when Brazil confirmed a case in São Paulo. Since then, governments across the region have taken an array of actions to protect their citizens and contain COVID-19's spread. This new coronavirus will spread widely in Latin America countries and knowledge about this new virus is necessary to adjust the reality of this new thread.

Coronavirus (CoVs) comprises a large family of zoonotic RNA-type viruses that belong to the Coronaviridae family. They can infect a variety of animals such as livestock, birds, pets, etc. [1,2] and can cause serious health problems, including cardiovascular, respiratory, gastrointestinal and neurological. In humans it can cause respiratory and gastrointestinal diseases, and it does so through symptoms ranging from a simple cold to a severe illness such as acute bronchitis, pneumonia, Pediatric Acute Respiratory Distress syndrome, coagulopathy, multi-organ failure, exacerbations of asthma, cystic fibrosis and even death [3,4].

On January 7, 2020, Chinese authorities identified a new virus in the Coronaviridae family as the agent causing an outbreak of severe pneumonia. It was named "novel coronavirus", 2019-nCoV. The World Health Organization has named the case with the acronym COVID-19 and the International Committee of Virus Taxonomy has named the virus causing the virus as coronavirus 2 associated with respiratory distress syndrome (SARS-CoV-2). SARS-CoV-2 is a new strain of coronavirus that has not been previously described in humans, is a betacoronavirus of the same subgenus as the Severe Acute Respiratory Syndrome virus (SARS-CoV).

The common circulation of COVID-19 can be isolated from 4% to 6% in children hospitalized for symptoms of respiratory tract infection, and around 8% in children in the outpatient settings. This virus has also been found to cause an exacerbation of asthmatic conditions [5-9].

Epidemiological management guidelines are NOT the objective of this document.

The main purpose of this publication is to present the suggestion of a management protocol by the Emergency Committee of SLACIP (Latin American Society of Pediatric Intensive Care) to confront the increase of cases at the local level in the context of a multinational collaborative work and adjusting to each of the realities and criteria of clinical management of the countries and clinical services that it is comprised of.

These recommendations may vary as our knowledge about the disease and the epidemiological situation in each country evolves and therefore can be updated.

Definition of cases

Cases to test: All people from risk area/s will be tested (localized transmission).

Suspected cases: Any person who presents:

- Fever and one or more respiratory symptoms:
 - Cough
 - Odynophagia
 - Difficulty breathing.

- No other etiology that fully explains the clinical presentation, and that in the last 14 days has been in contact with confirmed or probable cases of COVID-19 or has a travel record or has a travel record abroad.
- Or any person with acute respiratory disease and who is or has been in close contact with a confirmed or probable symptomatic case in the 14 days prior to the onset of symptoms.

The suspected case of COVID-19 should also be considered:

- All patients with severe acute respiratory disease requiring intubation upon admission to the Emergency Department, without another etiology that explains the clinical picture.
- And all patients with severe acute respiratory disease defined as: pneumonia, includes clinical and radiological diagnosis of pneumonia + any of the following:
 - Tachypnea according to age:
 - < 2 months: $\geq 60/\text{min}$
 - 2 - 11 months: $\geq 50/\text{min}$
 - 1 - 5 years: $\geq 40/\text{min}$.
 - $\text{Sat O}_2 < 92\%$ (ambient air).
 - Increase of infiltrates $> 50\%$ in 24 - 48 hours.
 - Altered consciousness.
 - Hemodynamic instability.

Probable cases: Suspected case whose laboratory results for SARS CoV-2 are inconclusive, Influenza A and B have been ruled out by PCR or are only positive for a generic coronavirus test.

Confirmed cases: Any person with PCR confirmation of positive screening for SARSCoV-2 [2].

Discarded cases: Case under investigation whose laboratory tests are negative for the detection of SARS CoV-2.

Laboratory criteria

Positive PCR screening and confirmation PCR in an alternative gene screening to also be positive.

General considerations about the triage and pre-triage system [10]

Although risk groups are well defined among children; Importantly, they can behave as a source of spread of infection, so special considerations must be taken in the clinical data flow.

If it is possible according to the structure of each country, to facilitate the decongestion of health care centers, it is recommended that together with a pre-triage and triage system, a teleconsultation model be implemented that allows the resolution of concerns of the popu-

lation from a reliable source, tele-assisted monitoring of mild cases that maintain isolation at home and direct cases according to clinical severity to the most appropriate centers, according to the availability of beds and specialists available and required.

Pre-triage

The objective is to establish two patient flows.

That of the “Suspected Cases of COVID-19” or respiratory cases on the one hand, and the rest of patients, or non-respiratory cases, on the other. Ideally, pre-triage should be carried out in facilities located outside the emergency area, taking care not to facilitate contacts with patients who attend emergency departments for other pathologies (trauma, asthmatic crisis, sepsis, fever without focus, etc.), because many of them could present comorbidities.

The personnel who carry out the PRE-TRIAGE must be protected with a mask and gloves. If possible, “suspected COVID-19 patients”, especially those with mild symptoms, may be evaluated in facilities located outside of Emergency department or areas created for this purpose and be referred to clinics specially designed for this purpose (Primary Care). With this objective, information systems such as “large posters” could be developed to immediately warn if it is a “probable case”.

It is suggested that the two patient flows do not share physical space and are attended by different healthcare teams. Therefore, if possible, 2 waiting rooms and 2 different sanitary equipment should be determined, always avoiding that these flows mix.

If it is not possible to perform pre-triage outside the ER or in the special area designated by the Hospital for this purpose, that is, the TRIAGE, then it will be carried out in the Pediatric Emergency Department, in the Emergency room or in some special area designated in the emergency service for this purpose. After finding out the patient’s reason for consultation, the questions will be limited to epidemiological criteria and related to the presence of respiratory and flu symptoms.

If the epidemiological and clinical respiratory criteria are positive, the health personnel will be notified and the patient will be escorted to the designated isolation area in the Emergency Department until he is treated, in order to avoid contact with other people. Personnel who do the transfer to the isolation area will wear a surgical mask (Surgical masks must be given to the family member and the child who presents with symptoms, before transferring them to another site). Once in the isolation area, health personnel can complete the triage and anamnesis to verify that the patient meets the epidemiological and clinical criteria.

Each hospital or emergency department must establish its own specific isolation procedure. Likewise, the establishment of a waste material disposal system that may be generated in said area, is recommended.

The family members or companions of the patient should not go to the isolation area, they will be informed of the procedures they must follow. In the case of minors or patients who require accompaniment, the patient will have the right to such accompaniment and the necessary measures must be taken for their protection by using adequate personal protective equipment, as set out in the point defined for such effect of this document.

General considerations on clinical management

Based on the available information, the incidence and severity of COVID-19 in children is less than that of adults, the severity varies according to age and ranges from 10.6% in children under 1 year of age, 7.3% between 1 at 5 years, 4.2% between 6 to 10 years, 4.1% between 11 to 15 years and 3% in those over 16 years of age [11].

It is important to have special measures in the emergency department to avoid contagions. Look at annex 1.

Personal protective equipment for emergency personnel [12,13]

In general, the cases under investigation should be kept in “contact and drop isolation”. Strict hand hygiene will be followed before and after contact with the patient and during and after the removal of personal protective equipment.

Personnel accompanying the patient to the isolation area will wear a surgical mask.

Personnel who take clinical samples, who attend probable or confirmed cases of testing or those who enter the isolation room (e.g. family members, cleaning personnel, etc.) must wear personal protective equipment for prevention of infection by microorganisms transmitted by drops and by contact that includes:

- Protective gown,
- Mask,
- Gloves and
- Eye protection.

In situations where the generation of aerosols is expected, which include any procedure on the airway, such as tracheal intubation, broncho-alveolar lavage, or manual ventilation, it is recommended as an additional precautionary measure to that previously described, the use of a mask with a filtration efficiency equivalent to FFP2 (N95) or higher. The number of people in the room should be reduced to a minimum to what is strictly necessary for patient care. Although it is not essential, if there is a possibility and if it is available, the patient can be cared for in a room with negative pressure.

For the mobilization of patients within the unit, specific areas should be designated according to the specifications of each center to avoid contact with contaminated patients, in the same way equipment (radiology equipment, ultrasound machine, electrocardiograph among others) and own supplies should be provided to avoid cross contamination.

The personnel present at this level of care must wear

- A highly effective N95 mask, or FFP2 or preferably FFP3 if available.
- Fitted full-frame eye protection or full face shield.
- Gloves.
- Long-sleeved waterproof gowns (if the gown is not waterproof and splashes of blood or other bodily fluids are expected to occur, add a plastic apron).

Scenario in the emergency room

It is known that when the outpatient sector is closed, patients go to the emergency room for common symptoms, flu, etc. For this reason, every doctor who is consulting any patient with mild symptoms should have protection from EPI, taking into account that pediatric patients in series such as that published by Dong, *et al.* [11] with cohorts on 2000 patients, up to 13% of positive patients may present as asymptomatic. Immunological immaturity has been proposed as one of the best evolution mechanisms in children. This presents us with the problem of a high number of asymptomatic patients who are probably positive or who present mild symptoms that in the midst of consultations may increase the rates of infection [14].

Treatment approaches according to clinical scenarios and clinical classification of the severity of COVID-19 infection in children [15]

A	Do they have symptoms of COVID-19?	Yes
B	Do they have risk factors?	No
C	Do they have warning signs?	No
D	Do they have respiratory failure or sensory disorder or hemodynamic instability?	No
E	Do they have Sat.O ₂ < 92% with tachypnea?	No

Scenario 1: Compatible cases (Group A).

Group A patients correspond to children with mild infection.

Clinical characteristics: Infection of the Upper Respiratory Tract (Fever, Fatigue, Cough, Odynophagia, Rhinorrhea, Nasal Congestion) can also be manifested by Abdominal pain, Diarrhea, Vomiting and Nausea.

Physical exam: Normal.

Treatment of group A patients

1. Outpatient management at home
2. Strict isolation
3. Fever: Paracetamol 15 mg/kg depending on fever
4. Ensure adequate hydration
5. Infants should continue breast feeding
6. Do not use salicylates in children under 18 years
7. Medical control if the fever persists more than 48 hours
8. Explain to the parents or guardians the following: If the patient has difficulty breathing, chest pain, bloody sputum, difficulty feeding, confusion or drowsiness, "he should urgently return to the healthcare center even if the 24 hours have not gone passed for his control".

A	Do they have symptoms of COVID-19?	Yes
B	Do they have risk factors?	Yes
C	Do they have warning signs?	No
D	Do they have respiratory failure or sensory disorder or hemodynamic instability?	No
E	Do they have O ₂ Sat < 92% with tachypnea?	No

Scenario 2: Cases compatible in children with risk factors (Group B).

Group B patients correspond to children with moderate infection.

There may be pneumonia (interstitial infiltrates, persistent fever, and dry and/or productive cough), moderate wheezing, with no evidence of hypoxemia, in patients who do not present any alarming symptoms.

This stage may be subclinical with radiological data of lung and tomographic lesions already present.

The patient with suspect + risk factor must be admitted to the Emergency Observation Unit for 6 hours. If clinical evolution is good, they are sent at their home with control.

Risk factors for complications in COVID-19:

- Age $\leq$ 1 year
- Chronic or debilitating disease
- Cardiopathies
- Chronic respiratory disease
- Mellitus diabetes
- Cancer
- Malnutrition
- Conditions with immune depression
- Chronic renal insufficiency
- Neuromuscular disease
- Social circumstances such as living very far from the health unit without reliable means of transportation.

Treatment of group B patients

1. Group criteria: Presence of one or more risk factors for complications.
2. Hospitalization conditions: isolation in an individual room in the ER.
3. Laboratory: Blood count, platelets, glycemia, urea, creatinine, GOT, GPT.
4. Chest X-ray in case of persistent cough:
 - a. COVID-19 compliant chest x-ray:
 - a. Bilateral infiltrates with interstitial or ground glass pattern, or
 - b. ARDS-compatible bilateral alveolar pulmonary infiltrates, or

- c. Unilateral multilobar infiltrate compatible with viral infection.
5. Liquids orally (supervised).
6. If they do not tolerate the oral route or drink little liquid, hydrate intravenously at a volume of 2/3 of the basal needs, except if they are dehydrated. In that case they remain in the observation unit for 8 to 12 hours.
7. If the clinical evolution after 12 hours is good with acceptable oral intake, discharge to the home is indicated.
8. If warning signs and symptoms are detected during the reevaluation, they go to Group C.
9. Assess giving Hydroxychloroquine, Azithromycin, Lopinavir/Ritonavir (See table 1).

A	Do they have symptoms of COVID-19?	Yes
B	Do they have risk factors?	Yes/No
C	Do they have warning signs?	Yes
D	Do they have respiratory failure or sensory disorder or hemodynamic instability?	No
E	Do they have O ₂ Sat. < 92% with tachypnea?	Yes/no

Scenario 3: Cases compatible and presence of warning signs and symptoms (Group C).

Group C patients correspond to children with severe infection.

Patients with respiratory symptoms that may be accompanied by gastrointestinal symptoms (diarrhea and vomiting).

There is progression to worsening during the first week of symptoms, with dyspnea and oxygen saturation less than 92%.

The patient must be admitted to the Emergency Observation Unit for 12 hours with strict control of vital signs every 3 hours.

Warning signs

- Difficulty breathing and/or
- Hypoxemia: O₂ saturation < 90% by breathing ambient air
- Dehydration or food rejection (in infants)
- Coughing up blood
- Difficulty feeding
- Confusion or drowsiness
- Crackles in lung auscultation
- Chest x-ray with pulmonary infiltrates
- Shortness of breath or increased work of breathing

- Hemodynamic compromise.

Treatment of group C patients

1. Level of care: Respiratory and contact isolation.

1. Hospitalization conditions in the observation unit: Isolate the patient individually; when this is not possible, gather several patients with the same diagnosis in the same room. Once the patient is compensated, transfer to a special room or area designated by each Hospital for these patients.
2. Laboratory: CBC, platelets, blood glucose, urea, creatinine, GOT, GPT, Electrolytes, C-reactive protein, CPK, troponins and BNP, fibrinogen, D-dimer, ferritin, arterial blood gas or O₂ saturation.
3. Chest x-ray.
4. Assess echocardiography (in patients with previous heart disease).
5. Clinical management.

- a. Vital signs control with Monitor, record every 2 hours.
- b. Intravenous hydration will be administered at a volume of 2/3 of the basal needs if the patient does not tolerate the oral administration, except if there are signs of dehydration. Regarding the administration of fluids, management should be conservative, avoiding fluid overload since it could worsen oxygenation.
- c. Oxygen therapy if the O₂ saturation is from 95% or less to ambient air, it will be administered through a nasal cannula if 3 liters/min of oxygen or less is required, or by means of a mask if > 3 liters/min of oxygen is required. Objective: keep O₂ Sat not less than 92%.

If there is no improvement or if there is a worsening with 7 liters/min, or FiO₂ of 60%, or Sa/FiO₂ of 300 for 4 hours, assess HFNC if it is available, if not, proceed to the management of group D.

- d. Start Oseltamivir orally if there is suspicion or evidence of influenza infection, if you have less than 48 hours of fever (dose: See annex 2), for 5 days or until confirmation of COVID-19.
- e. In case of wheezing: albuterol 2 shots per aerochamber every 20 minutes for 2 hours, then according to evolution. If not, move on to managing group D.

The administration of bronchodilators is recommended in pressurized form associated with a space chamber MDI to avoid the generation of aerosols, as long as its clinical utility is demonstrated with an initial therapeutic test.

Nebulized bronchodilators (continuous or intermittent) may be chosen when the patient does not improve with the treatment by aerochamber at a dose of 2 shots every 10 minutes, if available, it is recommended to perform it in a room with negative pressure or to do it in a single room. Nebulizations should always be avoided as much as possible. If this type of room is not available, they will be administered in a room or box for individual use with bathroom, with natural ventilation or independent air conditioning. The door to the room must always be closed.

- f. In case of Fever: acetaminophen 15 mg/kg (up to 500 mg).
- g. If there is suspicion of bacterial superinfection (Leukocytosis and elevation of CRP or PCT) start antibiotics according to national guidelines for the management of community-acquired pneumonia.
- h. Give Hydroxychloroquine, Azithromycin, Lopinavir/Ritonavir (See table 1).

A	Do they have symptoms of COVID-19?	Yes
B	Do they have risk factors?	Yes/No
C	Do they have warning signs?	Yes
D	Do they have respiratory failure or sensory disorder or hemodynamic instability?	Yes
E	Do they have O_2 Sat < 92% with tachypnea?	Yes

Scenario 4: Compatible case in a critical patient (Group D).

Group C patients correspond to children with critical infection

There is rapid progression to acute respiratory distress syndrome (ARDS) or respiratory failure, which may be accompanied by shock, encephalopathy, myocardial injury, heart failure, coagulopathy, acute kidney injury, and other manifestations of target organ damage.

The patient must be admitted to the Intensive Care Unit in strict isolation or continue treatment in the Emergency Room in the area for critically ill patients while obtaining a place in the PICU.

Indications for admission to PICU:

- Clinical evidence of severe respiratory distress: Expiratory complaint, generalized retraction, central cyanosis, nasal flutter, nodding, tachypnea.
- Inability to feed.
- $PaO_2/FiO_2 < 250$.
- $SAFIO_2 < 264$.
- O_2 Sat < 92% with $FiO_2 \geq 0.5$ (with mask with reservoir).
- Recurrent apneas.
- Clinical need for MV or AMV.
- Hemodynamic instability.
- Sensory disorder.
- Lung infiltrates in more than 2 quadrants.

Treatment of group D patients

1. Level of care: In an Intensive Care Unit or in the Emergency Room, critically ill patients while getting a place in the PICU.
2. Laboratory: Haemogram, PCR, Urea, Creatinine, Glycemia, GOT, GPT, Electrolytes, Blood Crisis, Blood Gas, Rhabdomyolysis Research: CK-Aldolase-LDH.
3. In severe patients, it is recommended to request, in addition, CPK, troponins and BNP, fibrinogen, D-dimer, ferritin and other data on HLH (hemophagocytic lymphohistiocytosis). Lumbar puncture will be assessed according to neurological symptoms.
4. Chest X-ray.
5. Echocardiography.
6. Treatment:
 - a. Oxygen therapy: Administer O₂ to maintain O₂ Sat. of 92% or more. If not, start HFNC if available in isolation Sector.
 - b. Intubation: IF the patient is critical and requires this procedure, it will be performed as follows:
 - i. Endotracheal tubes with a balloon will be used to prevent leakage, with balloon pressure < 25 cm H₂O.
 - ii. If necessary, the patient will be pre-oxygenated with an O₂ reservoir mask instead of self-inflating bag ventilation and will be performed with a rapid intubation sequence and by expert personnel to minimize the time and number of attempts of the intubation procedure.
 - c. Manual ventilation with mask and self-inflating bag: If possible, avoid ventilation with mask and self-inflating bag. If it must be used, it will be done with a high efficiency filter that prevents viral contamination, between the self-inflating bag and the mask, without hyperventilating and preventing leaks.
 - d. There should be conservative fluid management, since aggressive management can worsen oxygenation generating pulmonary edema (give a contribution of 2/3 of the basal needs, except if the patient is dehydrated).
 - e. Hypotonic serums are not recommended (nor starches nor jellies in case of resuscitation). In the case of resuscitation, it is recommended to use crystalloids (Ringer lactate or 0.9% saline), the use of starches or jellies is discouraged.
 - f. Avoid and/or limit aerosol-generating procedures as much as possible (Table 1).
 - g. Systematic administration of antibiotics is not indicated. It will be assessed based on the severity of the clinical picture and the suspicion of bacterial infection.

If there is suspicion of bacterial infection (leukocytosis and elevated CRP (c-reactive proteins) or PCT), start antibiotic therapy with intravenous cefotaxime + vancomycin [12].
 - h. Correct acidosis, hypoglycemia, hypocalcemia
 - i. Systemic corticosteroids: Not liberally recommended. Previous studies in patients with SARS have shown that they have beneficial effects if it is well used [16]. There are currents who support that the clearance of the virus has been delayed with indiscriminate use.

There is a recent Chinese consensus that if it is used at a low dose 0.5 to 1 mg/kg/day and for a short time of 3 to 5 days, it can be effective and without collateral damage [17,18].

In persistent shock after 24 hours, the administration of hydrocortisone should be considered for the treatment of possible associated adrenal insufficiency. Recently, the preliminary results have been reported, that Dexamethasone improves survival in COVID-19 by Oxford University. Dexamethasone reduced deaths by one-third in ventilated patients (rate ratio 0.65 [95% confidence interval 0.48 to 0.88]; p = 0.0003) and by one fifth in other patients receiving oxygen only (0.80 [0.67 to 0.96]; p = 0.0021) [19].

- j. If septic shock is suspected: (think when we have: * Hypotension (SBP < 5th percentile or > 2 SD below normal for age) or 2 - 3 of the following: * altered mental status; * tachycardia or bradycardia (HR < 90 bpm or > 160 bpm in infants and HR < 70 bpm or > 150 bpm in children); *slow capillary refill (> 2 seconds) or *hot vasodilation with preserved pulses; * tachypnea; *mottled skin or petechial rash or purpuric; *increased lactate, *increased PCT, *oliguria, *hyperthermia or hypothermia)

Start administration of saline 20 ml/kg bolus; repeat three or more times according to evolution.

If you reach a dose of 60 ml/kp of liquid infusion, start inotropics (Adrenaline or Noradrenaline as first-line drugs 0.05 - 2 ug/kg/minute).

If signs of shock persist, assess: Heart failure due to cardiomyopathy or Bacterial sepsis.

- k. The treatment with bronchodilators can be evaluated in cases of ARDS, septic shock, encephalitis, hemophagocytic syndrome and when there is severe bronchospasm with wheezing refractory. If there is severe bronchospasm or refractory to albuterol, give 2 shots with Aerochamber every 10 minutes with O₂ for 2 hours [20] and start intravenous corticosteroids.
- l. Oseltamivir: Neuraminidase inhibitors (Oseltamivir) have been used in cases of MERS-CoV and have been initially used in the COVID-19 epidemic in China. Its efficacy is unclear and has possibly been used for the treatment of influenza coinfection. At the present time it is not routinely recommended, except for suspected coinfection with influenza.
- m. There are arguments for the use of lopinavir/ritonavir: It has *in vitro* activity against coronavirus, its safety profile and interactions are widely known for the treatment of HIV. Lopinavir/ritonavir treatment will be considered in children with underlying pathology, even in mild cases and in children in groups C and D. It frequently has gastrointestinal adverse effects at the start of treatment (diarrhea, vomiting) (See table 1).
- n. Hydroxychloroquine + Azithromycin: Hydroxychloroquine plus Azithromycin 18 treatment (3 - 5 mg/Kp/day in 1 or 2 doses for 10 days) will be evaluated in severe group D children (< 6 years: hydroxychloroquine sulfate 6.5 mg/kg/day divided every 12 hours (max. 400 mg/day); > 6 years: hydroxychloroquine sulfate 10 mg/kg/day divided every 12 hours (max. 400 mg/day). Monitor hypoglycemia, hematological, musculoskeletal and eye toxicity [21] (See table 1).

Observation

Antiviral and antibiotic treatment decisions should weigh individual risks and benefits for the patient in question, taking into account considerations such as potential risk factors for disease progression, clinical evolution, and drug contraindications or interactions. Also must be confirmed by the infectology team at each hospital, due to the continuous change in the treatment of the Covid-19.

Classification		Treatment ¹	Comments
Group A		Symptom	
Group B	Without pneumonia	Assess hydroxychloroquine + azithromycin ± lopinavir/ritonavir ²	Control electrolytes and ECG previous and during treatment.
	With pneumonia	Hydroxychloroquine + Azithromycin ± Lopinavir/Ritonavir ²	Control electrolytes and ECG previous and during treatment.
Grupo C		Hydroxychloroquine + azithromycin ± lopinavir/ritonavir ²	Control electrolytes and ECG previous and during treatment.
Grupo D		Hydroxychloroquine + Azithromycin ± Lopinavir/Ritonavir ² or Remdesivir ³	Control electrolytes and ECG previous and during treatment.

Table 1: Indications to assess specific treatment in pediatric patients with COVID-19.

1. Doses and duration of treatment See annex; 2. Start preferably in the first 4 days of symptoms.

ANNEX 1. PEDIÁTRIC DOSIS

Hydroxichloroquine: 3-5 mg/kg/day for 5 to 10 days.

Administration: Administer preferably with food. The pill can be crushed and diluted in water or milk to give through nasal gastro tube .

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Azithromycin: 10 mg/kg the first day, then 5 mg/kg every 24 hrs for 4 days.

Lopinavir / Ritonavir: for 7 days.

Doses of oral solution

< 3 months: 300 mg/m²/dose (lopinavir); twice per day.

≥ 3 months and <15 Kg: 12 mg (lopinavir)/Kg/dose; twice per day.

15 to 40 Kg: 10 mg (lopinavir)/Kg/dosis; twice per day.

> 40 Kg: 400 mg (lopinavir) twice per day.

Remdesivir IV 3

200-mg loading dose on day 1, followed by a 100-mg maintenance dose administered daily on.

Special Considerations

When we have critically ill children with shock and with multisystem (>2) organ involvement (cardiac, kidney, respiratory, hematologic, gastrointestinal, dermatologic, or neurological), we must suspect in pediatric inflammatory multisystem syndrome temporally associated with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)(PIMS-TS).

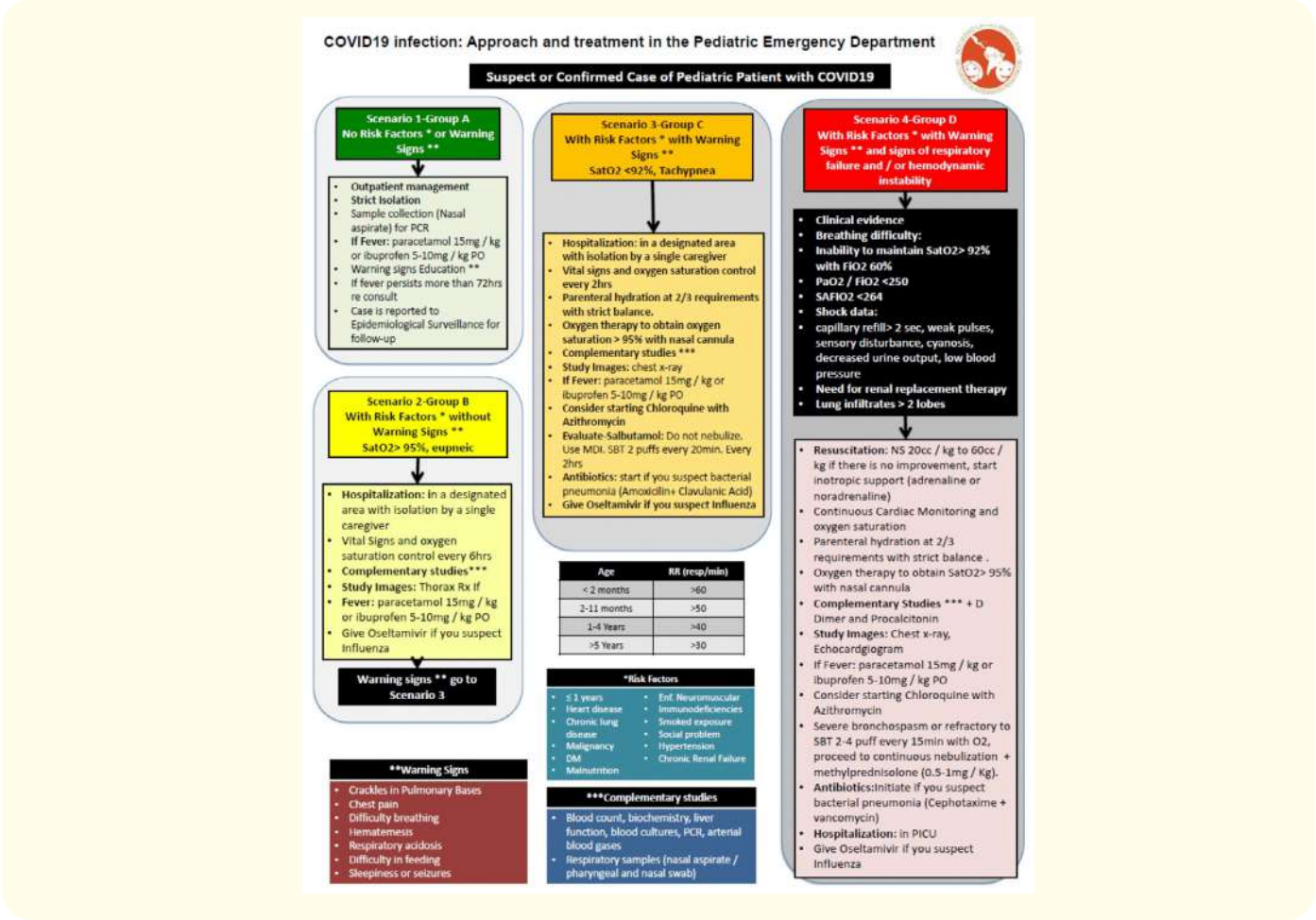
Case Definitions for PIMS-TS[22-24]

Children and adolescents 0–19 years with persistent fever> 24 hrs

AND two of the following:

- 1. Rash or bilateral non-purulent conjunctivitis or muco-cutaneous inflammation signs (oral, hands or feet).
- 2. Hypotension or shock.
- 3. Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including ECHO findings or elevated Troponin/NT-proBNP),
- 4. Evidence of coagulopathy (by PT, PTT, elevated d-Dimers).
- 5. Acute gastrointestinal problems (diarrhoea, vomiting, or abdominal pain). and
- 6. Laboratory evidence including: an elevated CRP level, ESR, fibrinogen, procalcitonin, ferritin, lactic acid dehydrogenase, or IL-6; elevated neutrophils;reduced lymphocytes; and low albumin.

Some patients may fulfill full or partial criteria for Kawasaki disease but should be reported if they meet the case definition for PIMS-TS.



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