



# Practical Guideline Management of COVID-19 in Children and Adolescents A Practical Up-to Date Guideline



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## Abstract

Sufficient high-quality data are unavailable to describe the management approach and guideline of COVID-19 disease in pediatric and adolescent population which may be due to mild presentation in most of cases and less severe complications than older ages.

World Health Organization was concerned with the establishment of an approved guideline to manage the increasing number of COVID-19 patients worldwide aiming to prevent or lessen COVID-19 global burden.

The clinical features have a wide spectrum starting from uncomplicated mild illness, mild-moderate pneumonia, severe pneumonia, acute respiratory distress syndrome, sepsis, septic shock, and multisystem inflammatory syndrome in children.

Many important definitions were developed to identify the COVID-19 case status including confirmed, suspected, and probable case.

Many laboratory tests may be beneficially done but reverse transcriptase – polymerase chain reaction (RT-PCR) for SARS-CoV-2 RNA is diagnostic.

Patient isolation and adequate intake of fluid and calories, antipyretics (preferably paracetamol), antibiotics (in secondary bacterial infections), and bed rest are the mainstay of approved supportive treatment. While oxygen supplementation may be added in moderate to severe cases; anticoagulation prophylaxis (enoxaparin) is strongly advised in children with certain situations where hypercoagulability state is identified, and therapy should be evaluated based on risk factors.

New approaches, drugs, and therapies are currently under research to manage COVID-19 pediatric and adolescent patients including antivirals (lopinavir/ritonavir, and favipiravir), remdesivir, tocilizumab, dexamethasone, convalescent plasma, and specific treatment of multisystem inflammatory syndrome in children (immunoglobulin, steroids, tocilizumab, anakinra, and aspirin).

The practical approach was summarized in a flow chart scheme to assist health care professionals to manage COVID-19 in children and adolescents within a rapid look though details are given in the text.

**Keywords:** Coronavirus, Diagnosis, Pediatrics, Treatment

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## Introduction

Since the appearance of first cases of the recent pandemic of severe acute respiratory syndrome coronavirus 2 (SARS- CoV-2) in China (which was called later as COVID-19), the world has been changed. Many data are available regarding adults unlike children and adolescence.<sup>(1)</sup>

Usually, transmission occurs due to direct inhalation of respiratory droplets of infected person or direct contact with surfaces

polluted with coronavirus. Less commonly, aerosol environmental generation by some medical procedures could be the cause of transmission like endotracheal intubation, cardiopulmonary resuscitation, bronchoscopy, open suctioning, and nebulization. Feco-oral transmission has not been confirmed yet in spite of the finding of the virus in stool of patients.<sup>(2)</sup>

Incubation period has a median of 5.1 days and very rarely it exceeds two weeks. The clinical features are just like traditional

acute viral infection of the respiratory tract including high temperature, sore throat, cough, dyspnea, and malaise. In the presence of co-morbidities and in some patients, the disease may progress to acute respiratory distress syndrome (ARDS), septicemia, septic shock, and even multisystem inflammatory syndrome in children (MIS-C) which has some similarity with Kawasaki disease.<sup>(3)</sup>

Most of pediatric and adolescent patients show a milder form of COVID-19 infection and they are usually asymptomatic which may be a negative point related to the increased burden of community transmission where children usually have a close contact with other adults including geriatric population whom have a severe course of COVID-19 in most instances.<sup>(4)</sup>

To confirm COVID-19 diagnosis, the virus should be detected in naso- or oropharyngeal swab and sometimes broncho-alveolar lavage using reverse transcriptase – polymerase chain reaction (RT-PCR). Other laboratory tests like C reactive protein and imaging studies including CT (computerized tomography) scan of the chest could be of help.<sup>(5)</sup>

Supportive treatment is the mainstay of management with anticoagulation strongly advised in children with certain situations where hypercoagulability state is identified as in diabetes mellitus and in adolescents as a prophylactic measure. Still prevention of infection spread is the cornerstone of COVID-19 management including isolation of exposed and diseased individuals (children and adolescents) and strict infection control approach involving activation of social distance and community hygiene are the only effective measures to break the transmission chain. Up to date, no vaccine is proved to be effective against COVID-19 and only few treatment measures are approved and confirmed by health authorities worldwide to treat affected patients. World Health Organization (WHO) takes the major global role to deal with the pandemic and new updated are always released along the way

of human struggle to control over the virus.<sup>(6,7)</sup>

**Aim:**

We tried to present the most recent practical updates of the management approach of COVID-19 pediatric and adolescent patients.

**Important definitions: (8)**

• Suspected case

Any of the followings:

• A patient with acute pulmonary disease (high temperature and at least one sign/symptom of a pulmonary illness, e.g., cough, and dyspnea), AND a history of travel to or settlement in an area reporting community spread of COVID-19 disease during 2 weeks prior to the onset of signs/symptoms.

• A patient with acute pulmonary disease (high temperature and at least one sign/symptom of a pulmonary illness, e.g., cough, and dyspnea), AND have been in contact with a confirmed or probable COVID-19 case (see definitions ahead) in the recent 2 weeks before the beginning of signs/symptoms.

• A patient with severe unexplained acute pulmonary disease (high temperature and at least one sign/symptom of a pulmonary illness, e.g., cough, and dyspnea), AND in need of hospital admission.

• Probable case

Any of the followings:

• A suspected case who has inconclusive testing for the COVID-19 virus.

• A suspected case who has no COVID-19 testing whatever the reason is.

• Confirmed case

An individual with laboratory confirmation of COVID-19 disease using Reverse transcriptase – Polymerase chain reaction (RT-PCR), irrespective of clinical signs and symptoms.

• Contact case

A contact is a person who experienced any one of the following exposures throughout 2 days before and 2 weeks after the appearance of signs/symptoms of a probable or confirmed case:

- Close contact (face to face) with a confirmed or probable case within a range at least one meter for more than quarter an hour.
- Direct contact and physical touch with a confirmed or probable case.
- Direct contact when taking care of an individual with probable or confirmed case without applying the least requirement of personal protective equipment.
- Miscellaneous: with identified risks like in patients with compromising immunity as in diabetes mellitus and cancer patients.

*Note:* for confirmed asymptomatic cases, the contact period is defined as 48 hours before throughout 2 weeks after the date by which the confirmatory laboratory sample was taken.

#### **Clinical presentation (clinical features):** (9,10)

A wide range of signs and symptoms are noticed.

##### 1) Uncomplicated Illness

At least one of the following:

- Uncomplicated upper respiratory tract viral infection without specific signs/symptoms including high temperature, cough, nasal congestion, sore throat, headache, malaise, and muscle pain, with no signs of dehydration, dyspnea, and septicemia.
- Gastrointestinal symptoms including vomiting, diarrhea, unexplained abdominal pain, and loss of taste.
- Others including anosmia, convulsion, impaired conscious level, and unexplained tachycardia.

##### 2) Mild and Moderate Pneumonia

Pneumonia presenting with cough, dyspnea, and tachypnea, with no signs of severe chest infection (see below).

##### 3) Severe Pneumonia

Child: cough, dyspnea, and one of the below:

- Central cyanosis.
- Respiratory rate (RR) >60/minute for <2 months old, >50/minute for 2-12

months old, >40/minute for 1-5 years old, and >30/minute for >5 years old.

- SpO<sub>2</sub> < 90% in room air.
- Severe respiratory distress.
- Mild pneumonia accompanied with inability to take oral feeding, lethargy, and fits.  
Adolescent: fever, cough, dyspnea, and at least one of the below:
- Respiratory rate (RR) > 30 breaths/minute.
- SpO<sub>2</sub> < 90% in room air.
- Severe respiratory distress.
- 4) Acute respiratory distress syndrome (ARDS)
- New or worsening respiratory symptoms within one week of known clinical insult.
- Chest imaging consistent with ARDS (bilateral multiple ground-glass shadows and/or infiltrating opacities, extensive consolidation, and pleural effusion).
- Respiratory failure not related to heart failure or even volume overload.

##### 5) Sepsis

Diagnosed by clinical measures and culture of specific specimens.

##### 6) Septic Shock

Diagnosis made clinically with disturbed level of consciousness and vital signs.

##### 7) Multisystem inflammatory syndrome in children (MIS-C)

Kawasaki-like disease with fever, conjunctival congestion, red or cracked lips, "strawberry tongue," rash, cervical lymphadenopathy, and swollen or erythematous hands and feet.

#### **Tests:** (11,12)

- All suspected cases should be referred to the nearest regional health center to perform the diagnostic test of reverse transcriptase – polymerase chain reaction (RT-PCR) for SARS-CoV-2 RNA. Preferred swab sample site is the naso- and/ or oropharyngeal area; and should be kept in viral transport media (VTM) on ice. In patients with mechanical ventilation, broncho-alveolar lavage (BAL) or endotracheal aspirate would be the recommended specimen and kept in

VTM on ice. Forced sputum production is not preferred and should be avoided due to risk of aerosol dissemination.

- Rapid serology kits may not be positive during first 7–10 days of infection and stay positive for several weeks following infection.
- Chest X-ray during early stage maybe normal or multiple small patches or plaques with interstitial haziness, mostly obvious in the lung periphery. Bilateral multiple ground-glass opacity and/or infiltrating shadows are found on deterioration, while in severe cases pulmonary consolidation is evident and pleural effusion may be seen.
- Computerized Tomography (CT) scan of the chest may shows ground-glass opacity and segmental consolidation in both lungs mostly peripherally. With more severe involvement, bilateral (rarely unilateral) multiple lobar lesions are seen.
- Chest Ultrasonography shows multiple B-lines, air bronchogram, pleural thickening, and consolidations.
- Coagulation studies including D-Dimer, prothrombin time (PT), partial thromboplastin time (PTT), and fibrinogen level (if possible). More severe disease with worse outcome is associated with higher D-Dimer levels.
- Infection markers including high erythrocyte sedimentation rate (ESR), C-Reactive Protein (CRP), and serum ferritin.
- Complete blood count (CBC) may show leucopenia and lymphopenia. Progressive lymphopenia occurs with disease progression.
- Liver and renal function tests are high in severe cases.
- Cardiac marker (serum troponin) could be elevated.
- Other organ markers including lactate dehydrogenase (LDH), creatinine phosphokinase (CPK), and myoglobin may be high.

### Treatment

Available treatment options up to date are as follows:

### 1) Supportive (13)

- Maintenance fluid (oral and/ or intravenous) and calorie intake.

- Antipyretics: paracetamol.

Plus:

- Antibiotics (broad-spectrum) when secondary bacterial infection occurs.

Plus:

- Oxygen supplementation in moderate to severe cases is aimed to prevent ARDS, organ failure, and secondary infection.

### 2) Steroids (14)

Steroid therapy is not indicated in majority of pediatric COVID-19 patients as they usually get well without severe complications. In adults, the RECOVERY trial showed a drop in mortality (within 28 days) in oxygenated or mechanically ventilated individuals when dexamethasone was used, while patients who did not need oxygen therapy and mechanical ventilation did not show benefits when using dexamethasone.

So that, dexamethasone must be avoided in patients who do not need a respiratory support.

Accordingly, here are the indications of dexamethasone:

- Respiratory support (oxygen therapy or assisted mechanical ventilation).
- Chronic illness that needs long-term steroid like in nephrotic syndrome, steroids (dexamethasone or other type) should be kept on.
- Current added illness that requires steroids, as in asthmatic patients.

### 3) Anticoagulation (15-17)

Venous thromboembolism (VTE) risk is high in COVID-19 adults. Unless contraindicated, consider prophylactic or therapeutic anticoagulation in all adult and adolescent individuals.

No specific guidelines are endorsed for pediatric COVID-19 cases. Hospitalized children having COVID-19 infection are assessed on case by case basis as follows:

- Send for hematological and oncological consultation for risk assessment and recommendations. Malignancy, obesity, and chronic heart diseases may be

- significant risk factors.
- consider VTE risk factors on hospital admission and re-evaluate every 2-3 days afterwards.
  - Unless contraindicated, enoxaparin prophylaxis is advised in children and adolescent confirmed COVID-19 cases.
  - Bleeding risk versus benefit must be evaluated on individual basis. Intracranial bleeding and presence of an active bleeding elsewhere may be considered as a contraindication, while caution should be experienced during lumbar puncture (within 24 hours), neurological procedure (within 24 hours), and coagulation disorders.
  - Alternative anticoagulation prophylaxis measures like early movement or physical procedures are recommended for all COVID-19 pediatric patients including those with contraindication to anticoagulation.

#### **Therapies currently under investigation for the treatment of pediatric and adolescent COVID-19 patients**

Treatment options should follow the scheme found in figure (1). The below-listed medications are still under investigation. The decision to use those under-research therapies should be made by the treating physician after full assessment of risk, benefit, clinical condition, comorbidities, and drug to drug interactions.

##### **1) Antiviral medications (13,18)**

The safety and effectivity of antivirals for treating COVID-19 have not been approved yet. Reliable data is absent to advocate the use of antiviral therapy in mild, moderate, severe, or critical COVID-19 illness. Examples of possible antivirals used in COVID-19 patients are lopinavir/ritonavir and favipiravir.

Lopinavir/ritonavir: oral tablets (200/50 mg)

Pediatric dosing:

Lopinavir/ritonavir: weight 7–15 kg: 12 mg/3 mg/kg; 15– 40 kg: 10 mg/2.5 mg/kg; > 40 kg: 400 mg/100 mg twice daily for 7-14 days.

(maximum daily dose lopinavir 400 mg/ritonavir 100 mg).

Adolescent and adult dosing:  
400/100 mg twice daily.

Duration of treatment: 7 days.

Favipiravir: oral tablets (200 mg)

Pediatric dose:

- 10-15kg: 200 mg twice on first day (maximum 400 mg/day). From the second day: 100 mg twice (maximum daily dose is 200 mg).
- 16-21kg: 400 mg twice on the first day (maximum 800 mg). From the second day: 200 mg twice (maximum daily dose is 400 mg).
- 22-35 kg: 600 mg twice on the first day (maximum 1200 mg). From the second day: 200 mg thrice daily (maximum daily dose is 600 mg).
- 36-45kg: 800 mg twice on the first day (maximum 1600mg). From the second day: 400 mg twice daily (maximum daily dose is 800 mg).
- 46-55kg: 1000 mg twice on the first day (maximum 2000 mg). From the second day: 400 mg in the morning, and 600 mg in the evening (maximum daily dose is 1000 mg).
- >55kg: for patients aged 16 and above use the adult dose, while use the above-mentioned dose of 46-55 kg for younger patients.

Adolescent and adult dosing:

1600 mg (8 tablets) twice on the first day. From the second day: 800 mg (4 tablets) twice daily for 7-10 days.

Duration of treatment: 7-10 days.

##### **2) Remdesivir\* (Intravenous infusion only) (19,20)**

It is a broad-spectrum antiviral drug (GS-5734; Gilead Sciences, Inc) and prodrug of nucleotide analog. On the first of May 2020, an emergency use authorization was given by US Food and Drug Administration (FDA) to allow remdesivir use in severe COVID-19 cases for pediatric and adult hospitalized patients. (19)

A new drug application (NDA) was submitted to the FDA in August 2020 for remdesivir. A phase 1b trial of an inhaled nebulized remdesivir was started in June

2020 to assess its potential benefit at the early phase of the disease as an outpatient treatment. (20)

Pediatric dose:

- <40 kg: 5 mg/kg as a loading dose given once then 2.5 mg/kg/day as a maintenance dose.
- $\geq 40$  kg: 200 mg as a loading dose given once then 100 mg as a maintenance dose.

Adult and adolescent dose:

Start with 200 mg as a loading dose given once then 100 mg as a maintenance dose.

Duration of treatment is 5-10 days.

Side effects:

- Elevated hepatic enzymes.
- Hypotension.
- Pharmacological interactions.
- Contraindicated with concomitant paracetamol use.
- Prolonged QT interval on ECG (electrocardiography).

Important notes of Remdesivir eligibility:

- Prior to initiation and daily during therapy, determine estimated glomerular filtration rate (GFR) adolescent and pediatric patients >28 days old. If GFR < 30 mL/minute, remdesivir is not recommended.
- Prior to initiation and daily during therapy, determine serum creatinine in full-term neonates (7-28 days old). If serum creatinine  $\geq 1$  mg/dL, remdesivir is not recommended.
- Prior to initiation and daily during therapy, determine hepatic laboratory testing. If liver enzymes are elevated, remdesivir is not recommended.
- The above-mentioned cautions should be considered and potential benefit versus risk should be assessed.

### 3) Tocilizumab (Intravenous infusion) (21,22)

It is an interleukin-6 (IL-6) inhibitor (biologic drug).

Usually, it is added to an antiviral medication for patients with high risk to develop cytokine storm who have the following criteria:

- IL-6  $\geq 3$  times upper normal limit.

- Serum ferritin >300 ug/L with doubling in 24 hours.
- Serum ferritin >600 ug/L at presentation plus LDH >250.
- D-Dimer > upper normal limit.

Dosing:

Children:

- < 30 kg: 12 mg/kg once (maximum 800 mg).
- $\geq 30$  kg: 8 mg/kg once (maximum 800 mg).

Adult ( $\geq 18$  years):

8 mg/kg once (maximum 800 mg).

Duration of treatment is one dose only. However, another dose could be considered after 8-12 hours if clinical deterioration continues. Typical response is expected within 48-72 hours with cessation of fever and improvement of oxygenation saturation.

Contraindications:

- Pregnancy
- Breastfeeding

Caution:

- Simultaneous use of more than one biologic.
- Live attenuated viral vaccines.
- Tocilizumab to anakinra conversion.
- C reactive protein & IL-6 levels are not reliable to measure the inflammation extent after tocilizumab treatment.

Serious side effects:

- Perforation of Gastrointestinal tract.
- Hepatitis.
- Infusion-related drug reaction.
- Anemia.

### 4) Steroids (Intravenous/ oral) (12,23)

Dexamethasone is preferred over other steroids and approved by RECOVERY trial. (12)

Alternatives:

- Prednisolone or methylprednisolone: during Breastfeeding and Pregnancy.
- Hydrocortisone: in premature infant (corrected gestational age <40 weeks).

Indication of steroids:

- Respiratory support (oxygen therapy or assisted mechanical ventilation).
- Chronic illness that needs long-term

steroid like in nephrotic syndrome, steroids (dexamethasone or other type) should be kept on.

- Current added illness that requires steroids, as in asthmatic patients.

Dosing:

Dexamethasone:

Children: 0.15 mg/kg/day given once daily.

Adult and adolescents: 6 mg/day given once daily.

Alternative steroids:

Prednisolone:

Children: 1 mg/kg/day given once daily.

Adult and adolescents: 40 mg/day given once daily.

Methylprednisolone:

Children: 0.8 mg/kg/day given once daily.

Adult and adolescents: 32 mg/day given once daily.

Hydrocortisone:

Children: 0.25 mg/kg/12 hours given twice per day for one week.

OR 0.5 mg/kg/day given once per day for 3 days.

Adult and adolescents: 10 mg/12 hours given twice per day for one week..

OR 20 mg/kg/day given once per day for 3 days.

Duration of treatment up to 10 days (unless indicated above).

Adverse events: (major)

- Hyperglycemia.
- Hypertension.

### 5) Convalescent plasma (24-26)

Although convalescent plasma has been used in some areas of the world to treat adult and adolescent COVID-19 patients, it has no official approval from World Health Organization (WHO) due to absence of related controlled trials. However, the administration of convalescent plasma in the early stage of severe COVID-19 disease has shown good recovery results.

The use of convalescent plasma in pediatric COVID-19 patients is still limited worldwide with lack of available large data. The decision to use convalescent plasma in children and adolescents should be evaluated case by case though severe adverse events are expected including anaphylaxis, hemolysis, and lung injury.

However, Food and Drug Administration (FDA) has declared an emergency use (EUA) of convalescent plasma recently on August 23, 2020 for severe (including dyspnea, respiratory rate  $\geq 30$  per minute, oxygen saturation  $\leq 93\%$ , lung involvement more than 50% within 1-2 days, and partial pressure of arterial oxygen to fraction of inspired oxygen ratio less than 300) or life-threatening (including septic shock, respiratory failure, and multiple organ dysfunction) COVID-19.

### 6) Ivermectin:

This drug was used for a long time for its anti-helminthic properties. In Iraq, a pilot study was performed under the supervision of Ministry of Health to show the effectiveness of ivermectin to decrease hospitalization when added to azithromycin and hydroxychloroquin (27). Also, the use of this drug was supported by some researchers (28) but denied by others. (29) Dose: a single dose of 200 mcg/kg orally, as an add-on therapy.

### 7) Specific therapy for MIS-C: (30-32)

**A) Immunoglobulins (IVIG):** given by intravenous infusion.

Indications:

- Kawasaki disease features.
- Coronary artery abnormalities.

Dose:

2 grams/kg, maximum dose 100 grams.

Adverse events:

- Infusion reactions.
- Aseptic meningitis.
- Hemolysis.

### B) Steroids (Intravenous/ oral)

Prednisone, prednisolone, and methylprednisolone are involved.

Indications:

- Kawasaki disease features.
- MIS-C.

Doses are given in pulses as 10-30 mg/kg daily for 1-3 days, then 2 mg/kg daily in divided doses until the condition becomes stable, and then followed by a taper.

Adverse events: (major)

- Hyperglycemia.
- Hypertension.

### C) Tocilizumab (Intravenous infusion)

It is a biological drug (IL-6 receptor blocker).

Indications:

- Fever continues >24 hours after steroids and/ or IVIG.
- Moderate and/ or severe presentation.

Dosing and adverse events:

See the above-mentioned details.

#### **D) Anakinra (subcutaneous, SQ and Intravenous infusion, IV)**

It is a biological drug (IL-1 Inhibitor).

Indications:

- Fever continues >24 hours after steroids and/ or IVIG.
- Moderate and/ or severe presentation.

Dose:

It is given 2-4 mg/kg (maximum 100 mg) SQ/ IV twice daily. The dose frequency may be increased to 3-4 times daily if poor response is encountered. In case of renal problems (creatinine clearance >30 mL/minute), consider dose adjustment. This drug is not dialyzable.

Clinical improvement is expected in 1-3 days.

Caution:

- Simultaneous use of more than one biologic.
- Live attenuated viral vaccines.
- Tocilizumab to anakinra conversion.

Side effects:

- Anaphylactic reaction.
- Compromised immunity.
- Short half-life (4-6 hours).
- Eosinophilia.
- Neutropenia.
- May be converted to tocilizumab but without concern.

#### **E) Aspirin (oral)**

It is a non-steroidal anti-inflammatory drug with antiplatelet, and anti-inflammatory function.

Indications:

All cases of MIS-C, not on other anticoagulation. However, prophylaxis of enoxaparin could be considered.

Use low dose (1-5 mg/kg/day) usually up to 81 mg/ day.

Adverse events:

- Gastrointestinal ulcer.

- Hemorrhage.
- Bronchospasm.
- Reye`s syndrome.

**Criteria of discharge:** (33,34)

- Absence of fever >3 days without antipyretics.
- Significantly improved respiratory symptoms.
- Obvious improvement of lung in imaging studies.
- No comorbidities or complications which require hospitalization.
- Consistent SpO<sub>2</sub> >94% without assisted oxygenation.
- Twice negative RT-PCR results, 48 hours apart (not mandatory).
- Discharge is better approved by multi-disciplinary medical team.

#### **Conclusion:**

The management of COVID-19 in children and adolescents has an approved part by WHO and other health authorities such as FDA including supportive treatment (adequate fluid and calorie intake, antipyretics, and antibiotics if secondary bacterial infection is suspected, plus oxygen therapy in advanced cases), dexamethasone in patients requiring respiratory support (oxygen), and anticoagulation prophylaxis and therapy (enoxaparin). However, the yet non-approved part of COVID-19 management which has therapies under current investigation includes antivirals, biological drugs (remdesivir, tocilizumab, and anakinra), steroids (other than dexamethasone), convalescent plasma, immunoglobulins, and aspirin. It is the duty of the treating pediatrician to evaluate the two parts of management (approved and under current investigation) for each individual case putting in mind the severity of the disease, co-morbidities, drug-drug interactions, expected adverse events, and available resources. The potential benefits of the management approach should outweigh the risks. However, the approved approach of pediatric and adolescent COVID-19 management should be followed strictly.

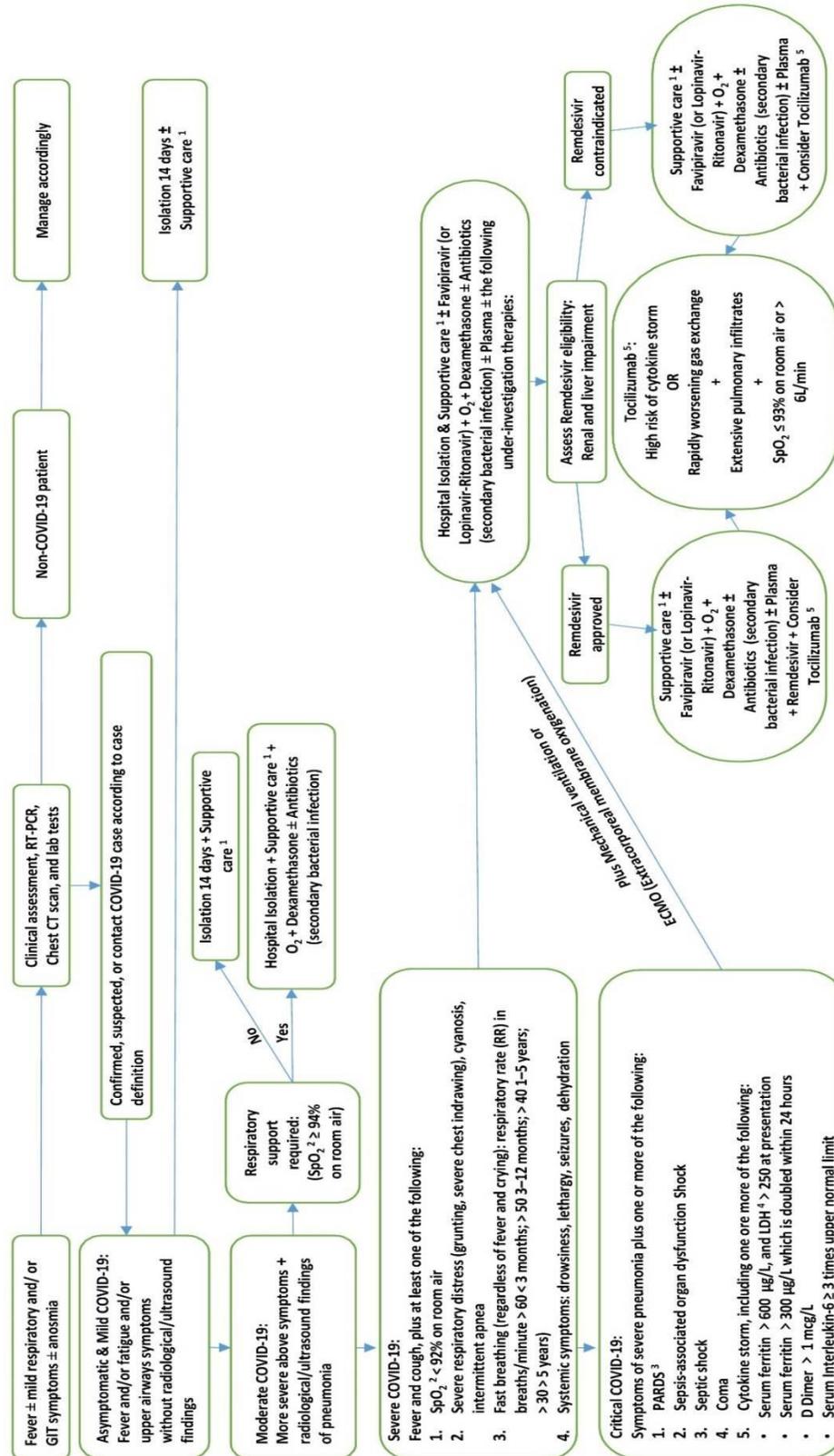


Fig. 1: Scheme of COVID-19 management in children and adolescents

\*Anticoagulation (Enoxaparin) prophylaxis should be evaluated in all COVID-19 children and adolescents unless contraindicated, especially for high-risk patients as malignancy, obesity, and chronic disease. For more details. See text please  
 †ivermectin could be used as an add-on therapy for hospitalized adolescents. Safety caution should be considered in infants < 6 months, or children < 15 kg. No pediatric experience has been released yet.

<sup>1</sup> Antipyretics (paracetamol 15 mg/kg/dose 6 hourly), maintenance fluid (oral and/ or intravenous) and calorie intake, vitamins, and tonics like vitamin C, D, and zinc.

<sup>2</sup> Oxygen saturations in arterial blood

<sup>3</sup> Pediatric Acute Respiratory Distress Syndrome.

<sup>4</sup> Lactate dehydrogenase

<sup>5</sup> Other biologic drugs could be used (such as anakinra).

**Conflict of interest:**

The authors declare no conflict of interest

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