Criteria for referral of pediatric SARS-CoV-2 infection: a real-life experience in the pandemic era

Carlotta Montagnani†, Elisabetta Venturini†, Manuela L’Erario‡, Chiara Tersigni§, Barbara Bortone¶, Leila Bianchi†, Francesca Menegazzo¶, Giuseppe Indolfi¶, Elena Chiappini†,3 and Luisa Galli†,3*

Abstract

A practical guidance on the management of children with COVID-19 to insure homogeneous criteria for referral to a higher-level facility, according to the disease severity, is pivotal in the pandemic era. A panel of experts in pediatric infectious diseases and intensive care at the tertiary-care Meyer Children’s University Hospital, Florence, Italy, issued a practical document shared with Tuscany hospitals. The rationale was to target the referral for those children at risk of requiring an intensive support, since the above mentioned hospital has the pediatric intensive care unit. Overall, 378 patients between 0 and 19 years of age were diagnosed with COVID-19 infection in the Tuscany region with 24 (6.3%) hospitalizations. Only three children were centralized to Meyer Children’s University Hospital according to reported criteria. Considering that appropriate referral criteria have been associated with reduced mortality in other conditions, our document might be useful to improve outcomes of children with COVID-19.

Keywords: SARS CoV-2, Children, Referral criteria, COVID-19

To the Editor,

severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the causative agent of coronavirus disease 2019 (COVID-19) [1]. Due to the spreading of SARS-CoV-2 in Italy, a guidance on the management of children with COVID-19 is needed in order to insure homogeneous criteria for referral to a higher-level facility, according to the disease severity. A panel of experts in pediatric infectious diseases and intensive care, currently in a multidisciplinary group for COVID-19 care at the tertiary-care Meyer Children’s University Hospital, Florence, Italy, issued a practical document that has been shared with Tuscany hospitals. The rationale was to target the referral for those children at risk of requiring an intensive support, since the above mentioned hospital has the pediatric intensive care unit.

Overall, 378 patients between 0 and 19 years of age were diagnosed with COVID-19 infection in the Tuscany region, up to 31 July 2020. Of these, 24 (6.3%) have been hospitalized in Tuscany hospitals [2]. In particular, 14 children have been admitted to Meyer Children’s University Hospital and only 3 of them (21.4%) were centralized from other hospitals (two infants because under 3 months of age and one 14 years old age with a genetic disorder). None of the children were admitted in intensive care unit.

In fact, according to the currently available data, COVID-19 in children usually presents as a...
asymptomatic/pauci-symptomatic disease. Asymptomatic cases do not require further evaluation unless clinical deterioration occurs. If present, clinical manifestations include fever (44–50%), dry cough (38%), asthenia. Other signs/symptoms are nasal congestion, rhinitis, headache, diarrhea, feeding difficulties [1, 3]. However, mild and severe cases are also described in children and disease severity can be classified as follows.

- **Asymptomatic**
- **Pauci-symptomatic/uncomplicated case:** fever and/or asthenia with mild upper respiratory signs, such as coryza, nasal obstruction.
- **Moderate case:** fever and/or asthenia and/or respiratory signs/symptoms, such as cough, mild distress with polypnea and/or difficulty in feeding, signs of dehydration.
- **Severe case:** fever and/or cough, plus at least one of the following:
  - SpO2 < 92% on finger pulse oximeter taken at rest
  - Tachypnea, in apyrexia and absence of crying (respiratory rate > 60 breaths/minute < 3 months; > 50 breaths/minute 3–12 months; > 40 breaths/minute 1–5 years; > 30 breaths/minute > 5 years).
  - Systemic signs of worsening: lethargy, inability to feed/drink, convulsions.
  - Shock or other organ failure requiring care.

It should be underlined that the early identification of risk factors and warning indicators for severe and critical disease is of paramount importance. These includes the following criteria:

- Age < 3 months.
- Underlying diseases (e.g. congenital heart disease, bronchopulmonary dysplasia, respiratory

### Table 1 Referral criteria for children with COVID-19

| Patient assessment | Supportive care | Setting of care | Referral |
|--------------------|-----------------|-----------------|---------|
| **Asymptomatic infection** | None | None | Discharge at home, refer to the family pediatrician with indications on isolation |
| **Pauci-symptomatic/uncomplicated case** | Oxygen saturation | None | In case of fever > 38 °C: paracetamol |
| **Moderate case** | Monitor vital signs (Bedside-PEWS) | Airway suction in case of obstruction | Hospitalization, isolation in single room with closed door |
| | - Blood tests: full blood count, C-reactive protein, erythrocyte sedimentation rate, procalcitonin, liver enzymes, lactate dehydrogenase, creatine phosphokinase, creatinine, electrolytes, hemogasanalysis, coagulation tests (prothrombin time, partial thromboplastin time, fibrinogen, D-dimers, INR) | - Oxygen therapy using nasal cannulas or facial mask with Venturi system (if oxygen saturation in air < 95%) | If the score (Bedside-PEWS) is not improved or increases after 2 h since oxygen and hydration support, refer the patient to a tertiary care hospital |
| | - Pulmonary ultrasound (if available) | - Intravenous access, adequate fluid and caloric intake based on hydration status | - Refer to a tertiary-care hospital if: |
| | - Chest x-ray in selected cases | - Give paracetamol in case of fever > 38 °C | - presence of alarm criteria |
| | - Other tests based on the clinical picture | | - needing for Venturi mask or High Flow Nasal Cannula to maintain SpO2 > 95% |
| | **Severe case** | Monitor vital signs (Bedside-PEWS) in order to early identify warning indicators: | Hospitalization, isolation in negative pressure room or, if not available, in single room with closed door |
| | - respiratory rate > 60 breaths/minute < 3 months; > 50 breaths/minute 3–12 months; > 40 breaths/minute 1–5 years; > 30 breaths/minute > 5 years | | - Intensive care admission indicated if warning signs does not improve after 2 h of patient support |
| | - SpO2 92–93% with FiO2 ≥ 40% | | Refer directly the patient to the tertiary care hospital |
| | - Poor mental reaction and drowsiness | | Referral should always be agreed with the infectious disease specialist |
| | - Increases of liver tests, muscular and cardiac enzymes | | |
| | - Metabolic acidosis | | |
| | - Bilateral interstitial infiltrates, pleural effusion on chest x-ray; rapid progression of radiological findings | | |
| | - Blood tests: full blood count, C-reactive protein, erythrocyte sedimentation rate, procalcitonin, ferritin, liver enzymes, lactate dehydrogenase, creatine phosphokinase, creatinine, electrolytes, hemogasanalysis, coagulation tests (prothrombin time, partial thromboplastin time, fibrinogen, D-dimers, INR, myocardial enzymes) | | |
| | - Pulmonary ultrasound (if available) | | |
| | - Chest x-ray | | |
| | - Computer tomography scan in selected cases | | |
| | - Other tests based on the clinical picture | | |
tract malformation, cystic fibrosis, hemoglobinopathies, severe malnutrition, abnormal hemoglobin, congenital or acquired immunodeficiencies, etc.)

- Respiratory rate increasing despite intravenous hydration and oxygen therapy with nasal cannula/ mask after 2 h of treatment.
- Poor mental reaction and drowsiness.
- Lactate increasing progressively.
- Bilateral or multiple lobe lung infiltrates, pleural effusion, rapid progression of radiological changes.
- Acute respiratory distress syndrome (ARDS) [4]

According to the present document, referral of patients with SARS-Cov-2 infection is not necessary in asymptomatic or uncomplicated cases. In moderate cases, referral should be established on the basis of criteria reported in Table 1. The bedside PEWS score is a useful tool to detect changing in the clinical picture [5]. It is appropriate in the presence of warning indicators or if the local hospital is unable to guarantee an isolation room or the level of care required. All severe cases should be early referred to a tertiary-care hospital with a pediatric intensive-care facility. Considering that appropriate referral criteria have been associated with reduced mortality in other conditions [6], our document might be useful to improve outcomes of children with COVID-19.

Abbreviations
ARDS: Acute respiratory distress syndrome; COVID-19: Coronavirus disease 2019; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2

Acknowledgements
Not applicable.

Authors’ contributions
CM, EV and MLE contributed to the study design and to the first draft of the manuscript; CT, BB, LB and FM contributed to drafting and reviewing the manuscript; GI, EC and LG contributed to the study conceptualization and reviewed the final draft of the manuscript. All authors read and approved the final manuscript.

Funding
None to declare.

Availability of data and materials
Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

Author details
1Infectious Diseases Unit, Meyer Children’s University Hospital, Florence, Italy.
2Intensive Care Unit, Meyer Children’s University Hospital, Florence, Italy.
3Department of Health Sciences, University of Florence, Florence, Italy.
4Direzione Sanitaria, Meyer Children’s University Hospital, Florence, Italy.
5Paediatric and Liver Unit, Meyer Children’s University Hospital, Florence, Italy.

Received: 10 October 2020 Accepted: 24 November 2020
Published online: 07 December 2020

References
1. World Health Organization. Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected. Interim guidance, 2020. Available at: https://www.who.int/docs/default-source/coronaviruse/clinical-management-of-novel-cov.pdf?sfvrsn=bc7da517_10&download=true. Last accessed: 15 August 2020.
2. Azienda Regionale di Sanità. Rapporto sui casi di infezione da SARS-CoV-2 in Toscana. https://www.ars.toscana.it/images/qualita_cure/coronavirus/rapporti_COVID-19/Rapporto_COVID-19_31_LUGLIO_2020_DEF.pdf Last accessed: 15 August 2020.
3. Centers for Disease Control and Prevention. Interim Infection Prevention and Control Recommendations for Patients with Suspected or Confirmed Coronavirus Disease 2019 (COVID-19) in Healthcare Settings. Available at: https://www.cdc.gov/coronavirus/2019-ncov/infection-control/control-recommendations.html. Last accessed: 15 August 2020.
4. Khemani RG, Smith LS, Zimmerman JJ, Erickson S. Pediatric Acute Lung Injury Consensus Conference Group. Pediatric acute respiratory distress syndrome: definition, incidence, and epidemiology: proceedings from the Pediatric Acute Lung Injury Consensus Conference. Pediatr Crit Care Med. 2015;16:33–40.
5. Panhurstam CS, Duncan HP, Joffe AR, Farrell CA, Lacroix JR, Middaugh KL, et al. Multicentre validation of the bedside paediatric early warning system score: a severity of illness score to detect evolving critical illness in hospitalised children. Crit Care. 2011;15:184.
6. Ostermann M, Vincent JL. How much centralization of critical care services in the era of telemedicine? Crit Care. 2019;23:423.

Publisher’s Note
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.