

Health-Care Organization For The Management and Surveillance of SARS-CoV-2 Infection in Children During Pandemic in Italy

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Research

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Abstract

Background: In comparison with adults, severe acute respiratory syndrome (SARS-CoV-2) infection in children has a milder course. The management of children with suspected or confirmed coronavirus disease (COVID-19) needs to be appropriately targeted.

Methods: We designed a hub-and-spoke system involving a Hub Centre to provide relevant healthcare information, based on the use of telemedicine and stringent admission criteria.

Result: Between March and April 2020, the Hub Centre managed a total of 119 children (62 males, 52%; median age, 5.5 years; interquartile range [IQR], 2; 10) with suspected or confirmed COVID-19. Of the 119 children, 90 were managed in cooperation with family paediatricians and 29 with hospital-based physicians. In total, 8 (6.7%) children were hospitalised, with a median length of hospital stay of 10 days (IQR, 8.5 days; range, 4–22 days).

Conclusion: case-by-case management allows a global evaluation in which the clinical condition is one determinant in medical decision-making along with the use of isolation to prevent the spread of COVID-19 among family members and cohabitants, and biocontainment measures. Large centres could coordinate paediatric COVID-19 cases through telemedicine, taking advantage of the generally milder presentation in children but also considering their dependence on adults and risk of infection spreading.

Introduction

The novel 2019 coronavirus disease (COVID-19) pandemic has disrupted social and economic life and created a global medical emergency. Due to the dramatic spread of the disease and the lack of rapid, reliable, and widely available diagnostic tests, social distancing, quarantine, and isolation measures have been applied so far.[1] Evidence concerning the risk and severity of COVID-19 in children remains relatively reassuring compared to the situation with adults.[2] Children have similar clinical hallmarks as adults; however, their symptoms are milder and the risks of complications, commonly observed in adults and particularly in elderly persons, are rare. However, relevant clinical studies have been diversely conducted, reflecting the heterogeneity of population enrolment criteria as well as of local management. In Wuhan, China, < 1% of 72,000 patients were found to be aged < 10 years.[3] One adolescent died but no lethal cases were reported in children in the age range of 0 to 10 years. In another series from China, infants and younger children had a higher risk of complications,[4] but most infants presented with mild disease. Severe and critical cases of COVID-19 have been confirmed in patients with coexisting conditions.[5] A more severe disease scenario was revealed from a case series in Spain reporting 41 children admitted with COVID-19-related respiratory symptoms and fever. Compared with children with similar clinical symptoms, that is, with suspected COVID-19 but whose test results were confirmed as negative, the general clinical conditions and symptoms were more severe, and a total of 4 children were referred to a paediatric intensive care unit, although no deaths were reported. However, it is difficult to reliably estimate what the risk is of a severe clinical outcome for children with COVID-19 in these different reports due, as noted, to heterogeneous enrolment criteria and disease management.[6, 7]. One recent report summarizes the clinical features of nine infants aged < 1 year with SARS-CoV-2 infection. All had been in contact with at least one affected family member and all eventually recovered. Clearly since no infant can take protective measures and children are a major source of infection, caregivers have to be protected. However, the authors did not report the rate of SARS-CoV-2 infection among the caregivers involved.[8] A COVID-19 diagnosis needs to be obtained quickly and isolation applied strictly; however, isolation is not easy to ensure for children admitted to hospital. Even quarantine at home can be highly challenging. Management of children is virtually impossible without the constant presence of a caregiver, particularly for infants and young children who need to stay in one room for at least two weeks (the usual period of COVID-19 positivity) and who are dependent on adults for their basic needs, including feeding and hygiene. Furthermore, two additional factors are

somewhat more worrying in relation to children. The first is that a child with few or no symptoms may spread SARS-CoV-2 infection to at-risk contacts, such as grandparents, and with a high probability to the direct caregiver, with highly dangerous consequences for such caregivers. The second is that certain children belonging to at-risk groups, particularly those with chronic conditions or immune suppression, may be at high risk (similar to the situation with adults) and should be closely observed clinically. Considering these factors, we designed a system for improved management of children exposed to or infected with SARS-CoV-2, in cooperation with primary care paediatricians (known as family paediatricians (FPs) in the Italian healthcare system) as well as with emergency care paediatricians. In the Italian public health system, all children are taken care of by FPs, who are responsible for disease prevention and care of all the children in a family. In general, the FPs have a complete knowledge of the entire family setting and particularly of the children, including their clinical history, immunisation record, and recent health status, as well as their social and living conditions.

A COVID-19 specific paediatric reference centre has been established to manage paediatric cases in the Campania region in Italy. This Hub Centre provides information to other healthcare institutions and primary care paediatricians, and coordinates medical services for children aged < 14 years. Here, we report the management pathway used in this Hub Centre and how it has performed thus far.

Methods

Setting and definitions

Campania is the most populous region in southern Italy, comprising approximately six million residents, of whom approximately 500,000 are children. In this setting, a hub-and-spoke system for the management of children aged < 14 years with COVID-19 was set up, with the Hub Centre coordinating all medical services involving children's admissions to a paediatric COVID-19-specific unit at the Hospital Federico II, Naples. The peak of COVID-19 infection occurred slightly later in the Campania region compared to the massive outbreak in Lombardy,[9] which allowed for more effective preparation. A suspected case was defined as a child with fever and respiratory symptoms AND exposure to COVID-19 through COVID-19-infected relatives or cohabitants or through direct contact with established infection OR as a child living within a designated red area (generally a small village or neighbourhood with fewer than 20,000 persons in which a cluster of SARS-CoV-2 infection had been found) and where extremely strict quarantine measures had been implemented. This definition was applied in cooperation with emergency hospital units and other hospitals. A child was admitted for hospitalisation to the specialised unit only if specific criteria in relation to COVID-19 were met and always after a telephone consultation with paediatric infectious diseases specialists to discuss and approve hospital admission.

Organisation of the management of children with or exposed to COVID-19 infection

A taskforce of 2 senior paediatricians and 6 paediatric residents was set up to work in the specialised unit. Residents in their 4th or 5th year of paediatrics formation were intensively trained at an early stage of the COVID-19 pandemic and enrolled in the taskforce. They updated incoming scientific information, oversaw a call centre, and were on call under the supervision of senior university paediatricians highly skilled in infectious diseases.

The unit consisted of 5 single rooms with strict isolation criteria and a triage room in which children were screened for admission in cases of suspected SARS-CoV-2 infection. Separate rooms for donning, doffing, and disposing of personal protective equipment were available. The call centre, which ran 24 hours a day 7 days a week, was made available to family physicians and other physicians to discuss medical assessments and for consultations. To establish SARS-CoV-2 criteria for admission, we reviewed the clinical criteria for hospitalisation in children with influenza-like-illness, pneumonia, or bronchiolitis and applied those relevant risk factors in determining a severe SARS-CoV-2 infection course and outcome (among children aged < 1 year). Hospital admission criteria for children infected with SARS-CoV-2 are

reported in Table 1. According to guidelines on childhood influenza symptoms and community-acquired pneumonia,[10, 11], these criteria include: severe clinical conditions or urgent need for hospital procedures, signs of respiratory distress, or the presence of underlying severe chronic diseases. In addition, even in the absence of clinical criteria, biocontainment criteria were applied. A child testing positive for COVID-19 was admitted if he/she was residing with cohabitants at risk due to older age or chronic diseases and because there was no alternative means to ensure home protective isolation, or if a child was in need of care and there were no available persons in that particular setting. Characteristics of the home in relation to COVID-19 management, specifically any options for effective protection of at-risk individuals, were also considered. The relevant criteria (globally defined within the context of hospitalisation for preventing the spread of COVID-19) were discussed on a case-by-case basis by the FP concerned and an expert at the call centre. This approach allowed more effective matching of relevant clinical and infection prevention criteria with the actual patient as well as information to be obtained concerning family composition and daily living conditions, resulting in optimal case management. The management decision resulting from a call to the call centre could include one of the following options: hospital admission to the specialised unit, COVID-19 triage to directly check the infection status and clinical conditions, quarantine at home, management at home of a suspected case or cases, management of a proven COVID-19 infected case or cases, or watchful waiting and update for re-evaluation within 24 hours. The triage process for COVID-19 included clinical evaluation and microbiological examination using a COVID-19 swab test. In all cases, feedback and follow-up measures were offered by the specialised unit to the FP concerned. Relevant information concerning this process was disseminated in collaboration with the Italian Society of Paediatrics and the organisational body responsible for FPs.

Table 1
Hospital admission criteria for children with SARS-CoV-2 infections

Characteristics	Indication for hospital admission
Fever < 3 months of age	Absolute
Aged < 12 months OR pre-existing risk factors or chronic diseases AND at least one of the following: <ul style="list-style-type: none"> ● Persistent fever for 3–5 days ● Oxygen saturation < 94% ● Extra-pulmonary complications ● Co-infections ● Pre-existing conditions (for example: diabetes mellitus, metabolic diseases, adrenal insufficiency, renal insufficiency, hepatic insufficiency, cystic fibrosis, ongoing immunosuppressive therapy) ● Prematurity < 34 weeks or Small for Gestational Age (< 2000 g) 	Relative
Congenital cyanotic heart diseases	Absolute
Persistence beyond 5 days of fever of high degree (> 38.5°)	Relative
Need for parenteral rehydration	Absolute
Oxygen saturation < 92% OR signs of respiratory distress or tachypnoea <ul style="list-style-type: none"> ● 0–2 months = 60 breaths/min ● 2–12 months = 50 breaths/min ● 1–5 years = 40 breaths/min ● > 5 years = 20 breaths/min 	Absolute
Myocardial enzymes, coagulation, liver indices, or lactate dehydrogenase alteration	Absolute
Lethargy, alteration in consciousness	Absolute
Seizures or neurological symptoms	Absolute
Biocontainment (risk of spreading SARS-CoV-2 infection to at-risk cohabitants in the absence of other isolation/quarantine measures)	Relative

Results

A total of 119 children (62 males, 52%; median age, 5.5; IQR 2; 10) were managed by the Hub Centre in the first month of activity (Figure). These included 90 children (mean age, 6 ± 4.1 years) managed in cooperation with FPs and 29 children (mean age, 6.9 ± 6 years) referred from other hospitals. A telephone call lasted a mean of 12 minutes and generally led to a shared decision between the experts within the Hub Centre and the family or hospital-based paediatricians. The main reasons for contacting the Hub Centre are reported in Table 2. At the beginning of the pandemic, most calls reflected a lack of knowledge and means to manage the resulting issues. In the subsequent phase, the reasons for calling became more specific. However, in many cases, the decisions and pathways for case management were not immediately clear. The major challenge was to make clear to the paediatricians calling that stopping the spread of infection was an issue as important to consider as a child's clinical conditions.

Table 2. Reasons for telephone consultations and decisions taken

Type of request	Total cases (n = 119)	Suspected cases (n = 91)	Confirmed cases (n = 28)
General information on how to manage a suspected COVID-19 child because of respiratory symptoms and fever, n (%)	79 (66)	79 (87)	0 (0)
Indications for microbiology examination, n (%)	42 (35)	41 (45)	1 (4)
Request for admission (general, not referring to clinical cases), n (%)	10 (12)	2 (2)	8 (29)
Indications for management of exposed children, n (%)	91 (76)	91 (100)	0 (0)
Management of COVID-19-positive children living with COVID-19-negative at-risk adults, n (%)	23 (19)	20 (22)	3 (11)
Request for admission (specific), n (%)	10 (12)	2 (2)	8 (29)
Prevention of infection (isolation/quarantine) generally, n (%)	119 (100)	91 (100)	28 (100)

Decisions taken following telephone consultations	Total cases (n = 119)	Suspected cases (n = 91)	Confirmed cases (n = 28)
Management of a suspected case, n (%)	91 (76)	91 (100)	0 (0)
Management of a confirmed case, n (%)	28 (23)	0 (0)	28 (100)
Watchful waiting, n (%)	109 (92)	89 (98)	20 (71)
Isolation of a COVID-19-infected child where there was risk to a cohabitant, n (%)	3 (2)	0 (0)	3 (11)
COVID-19 triage, n (%)	12 (10)	12 (13)	0 (0)
Admission to the paediatric COVID-19 specialist unit, n (%)	12 (10)	2 (2)	8 (28)

The decisions taken are listed in Table 2. The most common decision was to reassure the paediatricians concerning the low risk of contracting COVID-19 in a child with respiratory symptoms and fever who had had no exposure to SARS-CoV-2. The availability of a follow-up call was reassuring to FPs; however, further contact rarely occurred and was uneventful in most cases. In certain cases, swabs were obtained, often because of the presence of cohabitants at risk of infection and where isolation at home might be required. It was decided in such cases that SARS-CoV-2 infection in the child (the suspected index case) needed to be confirmed or excluded to determine whether a cohabitant needed home isolation. However, delays in obtaining swab results was an operational barrier. Often these were available only after 12 to 36 hours, during which time preventive measures against infection had to be applied either at the home or in the hospital. Furthermore, the presence of at-risk persons living in the home was an indication to separate a suspected SARS-CoV-2-infected individual from non-infected individuals but often this was not possible at the home and the child needed to be taken to hospital to be isolated. Another issue was the unknown COVID-19 disease status among the cohabitants concerned, which necessitated a temporary separation of all members in the family or the application of preventive measures, where possible, while awaiting the microbiological results.

Often the clinical symptoms of SARS-CoV-2-infected children were mild and did not meet the criteria for hospitalisation. We aimed to limit unnecessary hospitalisation. In many cases, there was a specific request to hospitalise a child, because there was little or no knowledge of management options. In such cases, hospitalisation and infection prevention were discussed initially with the FP and subsequently between the FP and the family. Multiple members within the family were often found to be infected. When the caregiver from the family (often the mother) had to stay in the hospital with the child, discussion occurred on how to organise the family and each member's role to find the best solution. Related to this, an issue for decision was the infection status of the person taking care of the child within the hospital isolation room, and this issue was openly discussed with the FP and by the FP in turn with the family before hospitalising the child. The caregiver had to be the mother, the father, or a relative, and that person was likely to be exposed or infected or at risk of becoming infected. The isolation room was organised as a mini-apartment, with food

and hygiene products provided, and the caregiver was responsible for feeding and cleaning the child to limit contact with healthcare workers. In certain cases, parents with COVID-19 were cared for by relevant specialists. Approximately 50% of the children included in this series had had exposure to relatives who tested positive to COVID-19. A total of 8 children were hospitalised (median age, 2 years; range, 0.2–5 years; mean, 0.6 ± 2.1 years) with a median length of hospital stay of 10 days (IQR, 8.5 days; range, 4–22 days). Specific reasons for hospitalisation are listed in Table 3.

Table 3. Main reasons for hospital admission in children with confirmed SARS-CoV-2 infection

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8
Age (years)	0.5	0.25	4	0.3	5	4	0.6	0.8
Sex	Male	Female	Female	Male	Female	Male	Male	Male
Overall clinical conditions	Moderate	Mild	Mild	Mild	Mild	Mild	Mild	Severe
Criteria for hospital admission								
Infection spread prevention	Yes	No	No	Yes	Yes	No	No	No
Clinical hallmarks	Respiratory distress Complex febrile seizure	-	Maculo-papular rash	-	Maculo-papular rash	Chest pain	Loss of appetite	Severe Sepsis
Risk factors	-	Prematurity Grade 2-IVH* Congenital cardiopathy Congenital syphilis	-	-	-	-	-	-
Contact of at-risk cohabitants with a confirmed case	Brother with autism	-	-	Grandfather with cancer	Brother with severe congenital cardiopathy	-	-	-
*IVH, intraventricular haemorrhage								

A 5-month-old boy (patient 1) was admitted with mild respiratory distress and had a relatively severe course of SARS-CoV-2 infection following a return of fever after a period of clinical improvement. He developed his first episode of complex febrile seizures, although a computed tomography CT scan of the head was negative, and had a long-lasting persistence of the virus, as shown on serial nasopharyngeal swabs (25 days). A 2-month-old preterm girl (born after 31 weeks of gestation, patient 2) with grade-II intraventricular haemorrhage, an atrial septal defect, congenital syphilis, and a previous episode of sepsis while in the neonatal intensive care unit, and who was admitted due to her age and

concomitant risk factors, showed relatively mild respiratory symptoms. Two other patients (patients 4 and 5) presented with skin maculopapular lesions, but both patients had an uneventful disease course. Patient 6, who had a mild infection course at home, tested positive to SARS-CoV-2 infection, using a nasopharyngeal swab, following two consecutive negative test results, and was referred to the unit for chest pain. A 9-month-old boy (patient 8) was admitted with a diagnosis of COVID-19, acute diarrhoea, and severe sepsis. During hospitalisation, a blood culture tested positive for extensive beta-lactamase-producing *Pseudomonas* and the infant received appropriate antibiotic treatment, fluid support, and blood transfusion. No respiratory supportive care was needed. A major reason for hospital admission in 3 of the 8 children was to prevent the spread of infection.

Discussion

Our clinical data support previous findings that children with COVID-19 do relatively better than adults. However, the risk of SARS-CoV-2 spreading, the unpredictable course of the disease, the fear associated with COVID-19, and the problems associated with feeding and cleaning an infant according to his/her age-related needs while awaiting clearance of viral infection make management of such cases difficult. Most children should be managed at home with little need for direct clinical management. This approach avoids the need for transportation and addresses issues related to wearing protective masks (difficult for a small child) and the risk of a SARS-CoV-2-infected child coming in direct contact with others. Taking a child for a medical visit may be challenging where lockdown conditions are implemented, and most of these infected children can be managed by telephone consultation or through telemedicine. However, in terms of preventing the spread of infection and the application of preventive measures among children, we found that different considerations for children compared to adults need to be considered, which affects the approach to the management of children and of families.

Given the lack of in-depth experience in dealing with this crisis, these considerations determined the management strategy and required a case-by-case decision involving the family and the FP in most cases. Biocontainment was identified as important a consideration as strictly clinical aspects. Of the few children admitted, only two had a relevant clinical issue, namely, complex seizures or severe general bacterial infection. All the other children recovered well, only requiring limited supportive measures. Similarly, follow-up at home, performed in collaboration with the FP, was shown to be easy and effective, and there were no major complications among the children. Hospitalisation in all other cases was predominantly directed at preventing the spread of COVID-19. Due to this finding, we amended the list of criteria for hospital admission of a child with COVID-19 infection to add biocontainment criteria. In most cases, hospitalisation was protracted while awaiting clearance of COVID-19. The need to keep a child in the hospital should be evaluated in relation to options for preventing the spread of infection that could be implemented in the home. Whatever decision is made should involve input from both the primary care physician and the family.

In conclusion, our data indicate that SARS-CoV-2 infection is clinically less severe in children than in adults. However, our data also indicate that the possibility of COVID-19 spreading, particularly due to infected children, is a major risk factor. Although preventing the possibility of COVID-19 spreading might not be considered a valid reason for admitting a child to hospital, it may be justified while awaiting a disease status confirmation.

This study had several limitations, specifically the relatively small sample size and the difficulty of generalising our results, given the heterogeneous organisation of healthcare systems in various settings. However, the conclusions appear to be broadly in line with results from other studies. Children appear to be at a relatively low risk of a severe outcome from COVID-19. They generate age-specific issues in terms of infection spread and disease management due to their specific needs and dependency on adult caregivers. These issues affect healthcare management and need to be addressed while taking into account the specific family setting, including the presence of persons at risk of COVID-19, the number of rooms at the home, the availability of toilets, and the opportunities for effective follow-up. Case-by-case

management should be applied at least in the present phase of the pandemic in a large centre, with the support of FPs working in cooperation with specialists in paediatric infectious diseases. With progressive understanding of the features of infection in children, criteria for management will become increasingly clearer.

List Of Abbreviations

coronavirus disease (COVID-19)

family paediatricians (FPs)

severe acute respiratory syndrome (SARS-CoV-2)

Declarations

Author contributions:

FN and AG conceived the study; FN, MP, LP, AC, GPC, EM and EV collected the patients' clinical data; FN, MP, LP, AC, GPC and EV analysed the data and wrote the paper; EB, ALV and AG revised the manuscript. All authors have seen and approved the version of the paper being submitted.

Compliance with Ethical Statements

Conflict of Interest:

The authors declare that they have no conflict of interest.

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This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent:

Informed consent was obtained from all individual participants included in the study.

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Extra data are available, by emailing the corresponding author at the address: franc.nunziata@gmail.com

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Figures

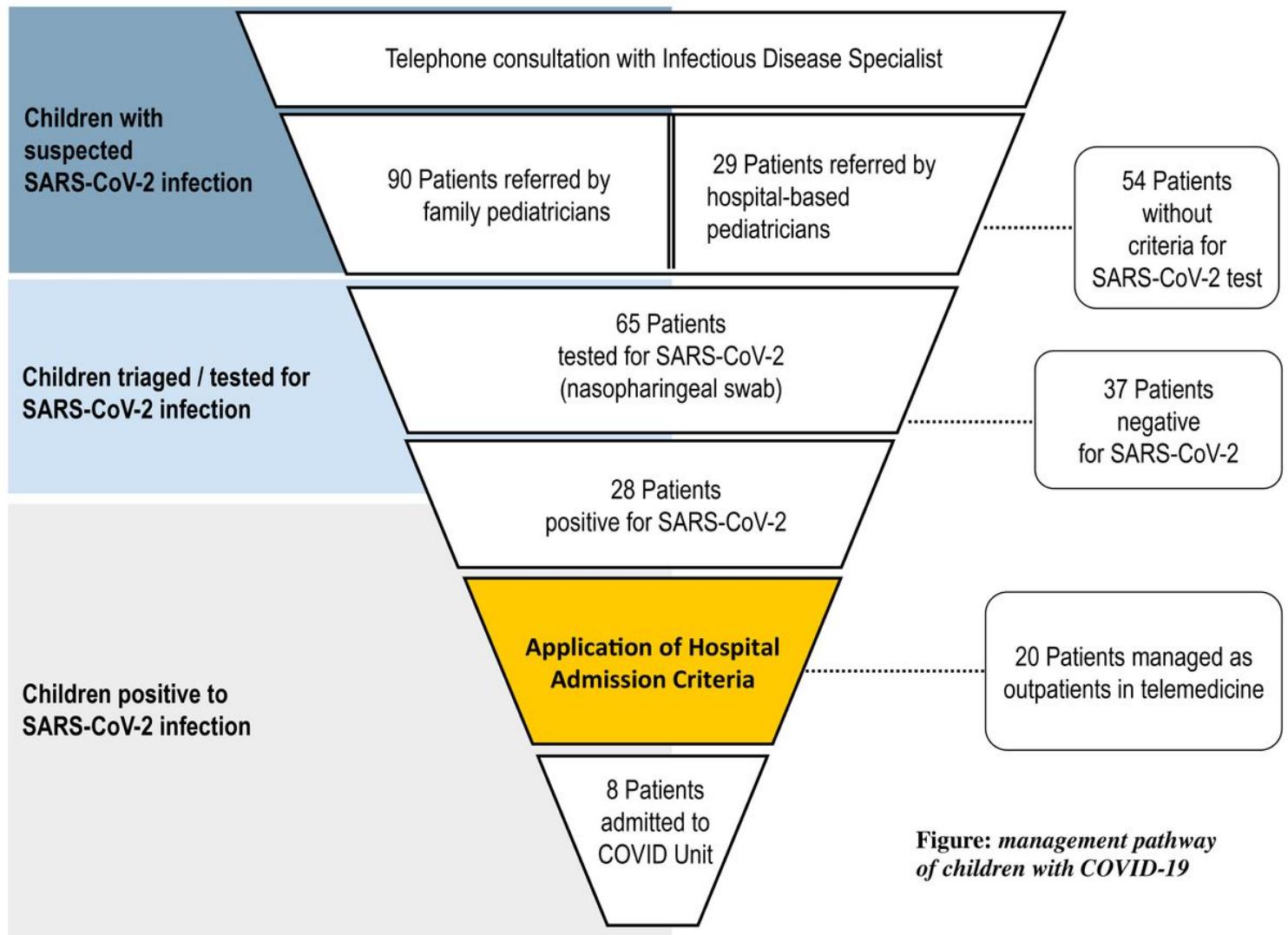


Figure: management pathway of children with COVID-19

Figure 1

management pathway of children with COVID-19