Original Article

Symptomatology and Outcome of Acute COVID-19 illness in Children at Faridabad, India

Priyanka Gupta, Onkar Singh Bhinder, Vipul Gupta, Abhinav Ahuja, Anil Kumar Pandey[1], R. N. Mandal Ravi

Departments of Pediatrics and [1]Physiology and Molecular Biology Laboratory, ESIC Medical College and Hospital, Faridabad, Haryana, India

Abstract

Introduction: The surveillance case definitions for coronavirus disease 2019 (COVID-19) in children adapted from adult guidelines emphasized the presence of fever and/or respiratory symptoms as the criteria for suspicion and testing. The clinical course of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection in Indian children is still not well described. **Materials and Methods:** This observational study was done at a dedicated COVID-19 tertiary care hospital of Haryana, India, between April 1, 2020 and December 31, 2020, with due approval of Institutional Ethics Committee. A total of 86 SARS-CoV-2 positive inpatient children in the age group of 1 month − 12 years were enrolled to outline the clinical course and outcome of acute illness longitudinally over initial 2 weeks of infection. Clinical management and hospital discharge policy was guided by public health authorities and prevailing scientific evidence which were updated and notified time to time as the pandemic evolved. Descriptive statistics were applied to analyze the study variables. **Results:** Majority children (48/86; 56%) remained asymptomatic throughout 2-week surveillance period, 35 (41%) suffered mild, 2 (2%) moderate, and 1 (1%) severe disease. All children had intact survival. Comorbid condition(s) were present in five (6%) children. Among infants and the subset of children with premorbid condition(s), the proportion of children suffering symptomatic illness (88% and 80%, respectively) and moderate-severe illness (25% and 40%, respectively) was quite high. Respiratory symptoms (68%) and fever (50%) were the most common symptoms. Gastrointestinal symptoms were present in 26% symptomatic children. Fever was the only symptom in 11% children; and 16% children had only gastrointestinal symptoms without any fever or respiratory symptom(s). **Conclusion:** Acute SARS-CoV-2 infection in children is commonly asymptomatic, or a mild illness with not only respiratory but also non-respiratory manifestations. Thus, a high index of suspicion for SARS-CoV-2 infection is required by the treating physicians in this subgroup of population as they might play an important role in virus transmission and amplification. In case the testing is deferred among asymptomatic contacts or children with mild symptoms, they may be presumed SARS-CoV-2 infected, isolated, and managed accordingly.

Keywords: Children, clinical course, COVID-19, outcome, SARS-CoV-2, symptoms

Introduction

The outbreak of 2019-novel coronavirus (nCoV) infection was declared a public health emergency of international concern on January 30, 2020. On February 11, 2020, the World Health Organization named this illness associated with 2019-nCoV as coronavirus disease 2019 (COVID-19) and the International committee on Taxonomy of viruses named this virus as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). It was declared a pandemic on March 11, 2020.

The initial published data in children were limited to case reports and small case series from a specific geographical region probably because the children were rarely tested for the virus during the early phase of the outbreak. This led to the belief that children are less affected with this infection and if at all affected, it is only a mild respiratory or influenza-like illness. Although published late, this is on record that even during the early phase of outbreak (between January 16 and February 8, 2020), 728 laboratory-confirmed and 1407 suspected pediatric cases were notified to the Chinese Center for Disease Control and Prevention.[1]

Submitted: 20-Aug-2021 **Revised:** 24-Nov-2021
Accepted: 24-Nov-2021 **Published:** 30-Dec-2021

Access this article online

Quick Response Code:

Website: www.actamedicainternational.com

DOI: 10.4103/amit.amit_138_21

Address for correspondence: Dr. Priyanka Gupta, Department of Paediatrics, ESIC Medical College and Hospital, NIT-3, Faridabad - 121 001, Haryana, India.
E-mail: drpriyankaguptakapil@gmail.com

How to cite this article: Gupta P, Bhinder OS, Gupta V, Ahuja A, Pandey AK, Ravi RN. Symptomatology and outcome of acute COVID-19 illness in children at Faridabad, India. Acta Med Int 2021;8:94-9.

During the first wave of pandemic, no separate surveillance case definitions existed for COVID-19 in children and the one used were adapted from the adult guidelines provided by public health/government and international agencies emphasizing the presence of fever and/or respiratory symptoms as the criteria for suspicion and testing.[2-10] The same have been endorsed by public health guidelines issued by Ministry of Health and Family Welfare, Directorate General of Health Services (EMR Division), Government of India[11] in the protocol for the management of COVID-19 in the pediatric age group. "Suspected case" is a patient with acute respiratory illness (fever and at least one sign/symptom of respiratory disease, e.g., cough, shortness of breath), and a history of travel to or residence in a location reporting community transmission of COVID-19 disease during the 14 days before symptom onset or having been in contact with a confirmed or probable COVID-19 case in the last 14 days before symptom onset or the absence of an alternative diagnosis that fully explains the clinical presentation. A person/child with laboratory confirmation of COVID-19 infection irrespective of clinical signs and symptoms is "Confirmed case" and a suspected case in whom RT-PCR could not be tested or inconclusive is "Probable case."

With the concerns of future waves of COVID-19 pandemic in India, this is extremely important to keep our boots strapped in a country with huge population and rapid rates of transmission, especially when effective drugs or vaccines are yet not available for this infection in children. This is well established now that the acute SARS-CoV-2 infection in children behaves like any other viral infection with multi-system manifestations and wide range of severity.[1,12-22] Despite the presence of published data worldwide, clinical course and outcome of acute SARS-CoV-2 infection in Indian children are not well described and there is only little published literature on this aspect limited to small datasets.[17,18] Ongoing surveillance is crucial in children as they might play an important role in virus transmission and amplification.[23] This study was done to fill this gap during the early phase of COVID-19 pandemic in India, as an attempt to learn the natural course of acute SARS-CoV-2 infection in children.

Materials and Methods

Study Design

Observational study.

Setting

ESIC Medical College and Hospital in Haryana, which served as a dedicated COVID-19 hospital during the study period.

Sample

All one-month to 12-year-old inpatient children with laboratory confirmed SARS-CoV-2 infection in nasopharyngeal/oropharyngeal swab sample using the reverse transcription polymerase chain reaction (RT-PCR) test.

Sample size

Eighty-six.

Study duration

Nine months (April 1–December 31, 2020).

Procedure

The study was approved by the Institutional Ethics Committee vide letter number 134/A/11/16/Academics/MC/2016/185 and the study participants were included with parental consent.

Three genes of SARS-CoV-2, i.e., E-gene (envelope coding gene), RdRP-gene (RNA dependent RNA polymerase gene), and N-Gene (Nucleocapsid encoding gene) were tested using Allplex™ 2019 nCoV Assay kit (Seegene Inc). Cycle threshold (Ct) value ≤35 was considered RT-PCR positive and >35 as negative. As an institutional and public health policy, asymptomatic children and those with mild illness were also admitted if their age was <1 year, had any co morbid condition(s) or lacked home isolation facilities.

Clinical severity of disease was categorized as "mild," "moderate," or "severe."[4-6] Uncomplicated infection without fast breathing and normal saturation (SpO2) ≥95% were categorized as "mild disease." Breathing rate of ≥60 in <2 months of age, ≥50 in 2–11 months of age, ≥40 in 1–5 year of age, and ≥30/min above 5 years of age were defined as fast breathing. Children with respiratory symptoms, fast breathing, and desaturation SpO2 <94% (range 90%–94%) on room air were categorized as "moderate disease." Those with signs of severe pneumonia, severe respiratory distress, SpO2 <90%, danger signs such as inability to feed, lethargy, unconsciousness or convulsions, septic shock, or multi-organ dysfunction were categorized as "severe disease."

Clinical management, hospital discharge, and isolation policy were guided by public health authorities and prevailing scientific evidence which were updated and notified time to time.[4-10, 24, 25] Clinical monitoring protocol included monitoring for temperature, SpO2, and signs of respiratory distress. No blood or radiological tests were done among asymptomatic children and those with mild disease. Symptomatic measures such as paracetamol, antihistaminic, nasal saline drops, and oral rehydration solution were prescribed in mild cases, and the treatment was individualized in moderate to severe ill patients. Antibiotic cover for pyogenic bacteria was provided in pneumonia cases (moderate-severe disease) because the clinical picture of bacterial pneumonia may overlap with COVID-19 and co-infections are not uncommon. Wherever required, one caregiver was allowed to stay with the child irrespective of his/her SARS-CoV-2 infection status following respiratory and hand hygiene practices. Lactational support was provided to all breastfeeding mothers.

Data pertaining to age, gender, any household contact, clinical symptoms, duration of each symptom, and comorbid condition(s) were recorded. Information about clinical symptoms was recorded first within 24 hours of admission and then prospectively till the discharge of patient. A clinical surveillance was maintained for a minimum of 2 weeks and the severity of disease was finally categorized as either "mild,"

"moderate," "severe," or "asymptomatic" after the acute phase of illness was over. For those discharged early, a telephonic follow up was maintained. Among symptomatic patients, a record of all investigations done and the treatment received was maintained.

Statistical methods

The anonymized data was compiled in the Microsoft Excel Software and analyzed by Epi Info Version 7. Descriptive statistics, namely frequencies and proportions were applied to summarize qualitative variables; mean-standard deviation for normal distributed quantitative data; and median-percentiles to summarize the quantitative data with skewed distribution.

Results

In this study, 86 laboratory-confirmed SARS-CoV-2-positive children were enrolled. The youngest one was 1 month old and eldest one was 12 years old. The median age of this surveillance cohort was 7 years (interquartile range [IQR]: 2–11 years). Majority of study population belonged to ≥5 year age group (57; 66.3%). There were eight (9.3%) infants (1 month to <1 year) and 21 (24.2%) children were 1 to <5 year old. Among these 86 children, 57 (66.3%) were male and 29 (33.7%) were female. There was some infected family member in 79 (91.8%) patients. A total of 83 (97%) children could be followed-up for complete 2 weeks duration to completely outline the clinical course during acute phase of SARS-CoV-2 infection.

Comorbidities in SARS-CoV-2-infected children and severity of COVID-19

Among 86, 5 (5.8%) patients had comorbid condition(s), namely allergic rhinitis; brain tumor with hydrocephalous; exogenous obesity; young infant born low birth weight with moderate anemia; and another young infant with congenital heart disease.

Overall, the majority of children were asymptomatic (48; 55.8%) with another 35 (40.7%) having mild disease. Only 2 (2.3%) had moderate and 1 (1.2%) had severe illness. In the subgroup of five children with comorbid condition(s), 4 (80%) were symptomatic, 2 (40%) with mild disease, and 2 (40%) with moderate illness requiring intensive care unit (ICU) care and oxygen therapy. Among eight infants, 7 (87.5%) were symptomatic, 5 (62.5%) with mild disease, and 2 (25%) with moderate COVID-19 illness requiring ICU care and oxygen therapy.

Symptomatology of COVID-19 in children

The frequency of symptoms and the mean duration of each symptom among symptomatic subset of infected children (n = 38) are presented in Table 1. Respiratory symptoms (cough, sore throat, rhinorrhea, and/or nose block) were present in 26 (68.4%) and fever in 19 (50%) symptomatic children. Four (10.5%) children had fever as the only clinical symptom of SARS-CoV-2 infection. Ten (26.3%) children had gastrointestinal symptoms (diarrhea, vomiting, and/or abdominal pain).

Table 1: Symptomatology of acute coronavirus disease-2019 in children

Symptoms	n=38, n (%)	Duration of symptoms (days), range	Duration of symptoms (days), median (IQR)
Fever	19 (50.0)	1-5	3 (1-3)
Cough	15 (39.4)	1-7	3 (2-4)
Sore throat	8 (21)	2-9	3.5 (2.3-4)
Rhinorrhea	3 (7.9)	2-5	3
Nasal stuffiness/block	1 (2.6)	7	7
Diarrhea	5 (13.1)	2-6	3 (2-4.5)
Vomiting	3 (7.9)	1-2	2
Abdominal pain	2 (5.3)	2-3	2.5
Fatigue/myalgia	3 (7.9)	1-10	6
Headache	2 (5.3)	2	2

IQR: Interquartile range

Six (15.8%) children had only gastrointestinal symptoms, without fever or respiratory symptoms**.** Gastrointestinal symptoms were not severe enough in any child to cause dehydration or need of intravenous fluids. No child had anosmia, lacrimation, conjunctivitis, or skin/mucosal rashes.

Clinical course of moderate-severe COVID-19 illness in children

None of the three moderate-severe ill children were given any specific antiviral, interleukin 6 (IL-6) inhibitor, remdesivir, tocilizumab or plasma therapy. The clinical course and treatment details in these three patients are as follows:

Patient 1

A 2-month-old, male child weighing 3.8 Kg, born small for gestational age at term, with birth weight 1900 g, following faulty feeding practices, had acute onset of fever and fast breathing for 5 days and positive nasopharyngeal reverse transcription polymerase chain reaction (RT-PCR) for SARS-CoV-2. The child had respiratory rate-62/min, mild chest indrawing and SpO2 92% in room air (improving to 96% on oxygen with headbox at flow rate of 5 L/minute) with crepitations heard on both sides of chest. Perfusion and blood pressure was normal along with normal cardiac, abdominal and neurological examination findings. Chest X-ray was suggestive of bilateral diffuse pneumonitis. Laboratory investigations revealed anemia and leukocytosis. Hemoglobin (Hb) was 8.5 g/dL, total leucocyte count (TLC) 26750/mm^3, neutrophil N (14.5%) and lymphocyte (L) 55.3%. Liver function tests (LFT), kidney function tests (KFT), electrolytes, and C-reactive protein (CRP) reports were normal, and blood culture was sterile. Child was given intravenous (IV) cefotaxime and amikacin for 7 days; and oral azithromycin for 5 days. Oxygen could be tapered and stopped by day 3rd of treatment the child was discharged after 8 days of inpatient stay after confirmation of negative SARS-CoV-2 RT-PCR status on day 7 of admission.

Patient 2

A 2-month-old, male child, weighing 4 Kg, with congenital heart disease (ostium secundum atrial septal defect with ventricular

septal defect and patent ductus arteriosus) admitted in view of fast breathing for 4 days and positive nasopharyngeal RT-PCR for SARS-CoV-2. The child was afebrile, had respiratory rate 54/min, chest indrawing and normal SpO2 in room air. Bilateral crepitations and systolic cardiac murmur were noted on auscultation. Liver was palpable 4 cm below right costal margin. The chest X-ray showed cardiomegaly and findings of bilateral diffuse pneumonitis. Laboratory investigations documented normal blood counts, hemoglobin, LFT, KFT, and CRP. Blood culture was sterile. The child was given oxygen with nasal prongs at the rate of 2 L/min for the clinical signs of respiratory distress and heart failure. IV amoxycillin + clavulanic acid and oral azithromycin was given for 5 days along with measures for heart failure in the form of furosemide and digoxin. Oxygen could be stopped by day 4th of treatment and SARS-CoV-2 RT-PCR on day-7 of admission was negative. The child was discharged after 14 days of hospital stay once cardiac status was stable.

Patient 3

A 10-year-old boy, weighing 24 Kg, admitted with symptoms of dyspnea and fast breathing for 4 days with positive nasopharyngeal RT-PCR for SARS-CoV-2. He had a history of short duration fever and mild cough lasting 2 days in the preceding week. The child was afebrile at the time of admission, heart rate − 110/minute, respiratory rate − 28/minute, SpO2 70% in room air (improving to 94% on oxygen with mask at rate of 8 L/min) and BP-91/51 mm Hg. Systemic examination including cardiac and respiratory system examinations were normal. Chest X-ray was suggestive of pneumonitis. Blood investigations documented raised LDH-1188 IU/L, mild elevation in SGOT-54 IU/L, and mild elevation in SGPT-67 IU/L. IL-6 levels could not be done but the blood counts, hemoglobin, LFT, KFT, electrolytes, CRP, procalcitonin, ferritin, and d-dimers were in normal range. Workup for dengue fever and malaria were negative, and blood culture was sterile. Child had to be given inotropic support for 2 days to maintain perfusion. He was given IV dexamethasone (5 days) and low prophylactic dose of enoxaparin (5 days) along with IV ceftriaxone (7 days) and oral azithromycin (5 days). Oxygen requirements abated by day 3rd of admission and the child was discharged after 8 days of hospital stay with confirmation of negative SARS-CoV-2 RT-PCR on day 7 of admission.

Duration of hospital stay

The inpatient stay varied from 1 to 17 days (median 9 days, IQR: 7-11) which was dependent not only on the severity and clinical course of illness but also on many social factors such as the facility for home isolation, comorbid condition(s), and the prevailing public health guidelines. The duration of hospital stay was ≤3 among 6 children, 4–7 days among 19 children, 8–10 days among 34 children, 11–14 days among 23 children, and >14 days among 4 children.

Discussion

Up to 90% children acquire SARS-CoV-2 infection from some infected family member, though the source of exposure still remains uncertain in many.[13-20,26-29] In the present study, 92% children belonged to a household cluster of SARS-CoV-2 infection and the source of exposure was unknown in rest 8%.

Most of the studies and reviews describe decent recovery rates in children with COVID-19.[1,12-20,26-34] Fatal outcomes are rare with reported mortality rates ranging from 0.0018 to 0.7% in various large datasets and systematic reviews.[12,15,19,27,28,31,33,34] In the present study, all children (100%) had an intact survival.

There is a wide variability in the description of proportion of asymptomatic cases and severity of SARS-CoV-2 infection due to variable local testing guidelines, hospital admission criteria, variable study designs, inclusion/exclusion of neonatal age group, and variable upper age limit of study participants. Various datasets describe that 6%–58% of SARS-CoV-2 infections in children are asymptomatic.[1,12-18,20,27-34] In the present study, 48 (56%) children were asymptomatic admitted either due to the lack of home-isolation facilities or association with another high-risk factor. Worldwide published literature and a few published data from India describes that 16%−50% infections are mild and 0.9%–4.9% children suffer severe-critical illness.[1,12,14,17,18,20,29-31,33] Up to 8% SARS-CoV-2-infected children require ICU admission[15,16,19] which again depends on the ICU admission criteria. In the present study, 35 (41%) children had mild disease, two (2.3%) children suffered moderate, and one (1.2%) child suffered severe COVID-19 illness. Three (3.5%) children with moderate-severe illness required ICU care, all three settled on free flow oxygen therapy and no one requiring any invasive or noninvasive ventilatory support but the one (1.2%) requiring ionotropic support.

Most of the studies and systematic reviews report a greater number of infected males than females,[1,12-20,27-31,33,34] hypothesizing that there might be some gender predisposition to SARS-CoV-2 infection. Some large datasets found male gender, younger age and preexisting comorbid conditions(s) to be risk factors for severe disease and ICU admission.[15] In the present study, male:female ratio among SARS-CoV-2-infected children was around 2:1. Comorbid condition(s) were present in 6% children. Among infants and the subset of children with premorbid condition(s), the proportion of symptomatic illness (88% and 80%, respectively) and moderate-severe illness (25% and 40%, respectively) was quite high. However, with a modest sample size and small number of recorded outcomes, no reliable statistical measure could be applied to the study relationship of severity of illness with age, gender, and comorbidity status.

Respiratory symptoms (such as cough, sore throat, rhinorrhea, and nose block) and fever are the two most common symptoms, reported in more than 32%−79% and 25%−82% SARS-CoV-2-infected children, respectively.[12-16,19,20,27-29,31-34] Gastrointestinal symptoms including diarrhea may be seen in 4%−16% and vomiting in 3%−11% infected children.[12,14,16,19,20,27-29,31-34] Beside respiratory and gastrointestinal symptoms, fatigue, myalgia and headache

are other common symptoms noted in up to 23% and 28% children, respectively.[12,14,16,18-20,27,28,31,32,34] Symptoms such as anosmia, lacrimation, skin rash, and mucosal rash are infrequently reported.[14,16,28,32] Non-respiratory and unusual symptoms could have been missed in the studies with small sample size.[26,30] A large multi-national, multi-centric large dataset from 21 countries and 77 institutions in Europe[15] found that among 582 RT-PCR confirmed SARS-CoV-2 infections in children, 40 (7%) had only gastrointestinal symptoms, 16 (35%) among them not even having accompanying fever. A Korean data also described one child who had loss of taste as the sole symptom of SARS-CoV-2 infection.[20]

Little is published about the symptomatology of acute COVID-19 illness among Indian children. A small hospital-based Indian data from Pune, Maharashtra, India[18] described 50 SARS-CoV-2-infected children, 21 being symptomatic. Fever was present in 81% and respiratory symptoms were present in more than 38% children. In the present study, respiratory symptoms were most common, present in 68% symptomatic children, followed by fever in 50% symptomatic children. Fever was the only symptom in 11% symptomatic children. Gastrointestinal symptoms were present in 26% symptomatic children. Many (16%) children had only gastrointestinal symptoms, without fever or respiratory symptoms.

On cannot learn the natural history of any disease in a cross-sectional hospital-based study, more so when many asymptomatic and mild cases are being self-managed at home missing attention. Only a very few studies followed-up the infected asymptomatic and symptomatic children longitudinally to outline the clinical course of acute illness.[16,20] In the present study, an attempt was done to get informed of all the new symptoms developing during the acute phase of SARS-CoV-2 illness by doing a longitudinal follow-up of children over complete 2 weeks. However, the risk for developing multi-system inflammatory syndrome which is a rare complication of SARS-CoV-2 infection in children seen 2 − 6 weeks after the acute infection could not be estimated. With a modest sample size and recording a limited number of variables, analysis could not be done for the severity of disease with variables such as age, gender, and comorbidity status. Despite these limitations, this preliminary data from our region may serve a guide for resource and workforce planning. Systematic reviews on the Indian data accumulated over the time may throw more light on this subject.

Conclusion

This study validates that the mild illness with non-respiratory symptoms is not uncommon in children with SARS-CoV-2 infection. Suspicion and diagnosis of COVID-19 in pediatric age group based on respiratory symptoms and/or fever alone may be misleading. Cases with predominant non-respiratory symptoms are likely to get missed unless a high index of suspicion is kept by the treating physician. If case the testing is deferred among asymptomatic contacts or children with mild symptoms, such children must be presumed SARS-CoV-2 infected, isolated, and managed accordingly to prevent community spread.

Acknowledgments

We express our gratitude to the Dean of our institution, Prof (Dr) Asim Das for all the logistic and administrative support.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Dong Y, Mo X, Hu Y, Qi X, Jiang F, Jiang Z, *et al.* Epidemiology of COVID-19 among children in China. Pediatrics 2020;145:e20200702.
2. World Health Organization. Clinical Management of Severe Acute Respiratory Infection (SARI) When COVID-19 Disease is Suspected. Interim Guidance. Available from: https://www.who.int/docs/default-source/coronaviruse/clinical-management-of-novel-cov.pdf. [Last accessed on 2020 Mar 20; Last updated on 2020 Mar 13].
3. CDC Health Alert Network. Updated Guidance on Evaluating and Testing Persons for Coronavirus Disease 2019. Available from: https://emergency.cdc.gov/han/2020/HAN00429.asp. [Last accessed on 2020 Mar 28; Last updated on 2020 Mar 08].
4. Directorate General of Health Services (EMR Division), Ministry of Health and Family Welfare, Government of India. Revised Guidelines on Clinical Management of COVID-19. Available from: https://www.mohfw.gov.in/pdf/RevisedNationalClinicalManagementGuidelineforCOVID1931032020.pdf. [Last accessed on 2020 Apr 01; Last updated on 2020 Mar 31].
5. Directorate General of Health Services (EMR Division), Ministry of Health and Family Welfare, Government of India. Clinical Management Protocol: COVID-19. Version-3; 13 June, 2020. Available from: https://www.mohfw.gov.in/pdf/ClinicalManagementProtocolforCOVID19dated27062020.pdf. [Last accessed on 2020 Jun 15].
6. Directorate General of Health Services (EMR Division), Ministry of Health and Family Welfare, Government of India. Clinical Management Protocol: COVID-19. Version-4; 27 June, 2020. Available from: https://www.mohfw.gov.in/pdf/ClinicalManagementProtocolforCOVID19dated27062020.pdf. [Last accessed on 2020 Jun 30].
7. Ravikumar N, Nallasamy K, Bansal A, Angurana SK, Basavaraja GV, Sundaram M, *et al.* Intensive care chapter of Indian academy of pediatrics. Novel coronavirus 2019 (2019-nCoV) infection: Part I – Preparedness and management in the pediatric Intensive Care Unit in resource-limited settings. Indian Pediatr 2020;57:324-34.
8. Balasubramanian S, Rao NM, Goenka A, Roderick M, Ramanan AV. Coronavirus disease 2019 (COVID-19) in children – What we know so

far and what we do not. Indian Pediatr 2020;57:435-42.
9. Sankar J, Dhochak N, Kabra SK, Lodha R. COVID-19 in children: Clinical approach and management. Indian J Pediatr 2020;87:433-42.
10. Kuttiatt VS, Abraham PR, Menon RP, Vaidya PC, Rahi M. Coronavirus disease 2019 in children: Clinical & epidemiological implications. Indian J Med Res 2020;152:21-40.
11. Directorate General of Health Services (EMR Division), Ministry of Health and Family Welfare, Government of India. Protocol for Management of Covid-19 in the Paediatric Age Group. Available from: https://www.mohfw.gov.in/pdf/ProtocolforManagementofCovid19inthePaediatricAgeGroup.pdf. [Last accessed on 2021 Apr 25; Last updated on 2021 Apr 20].
12. Lu X, Zhang L, Du H, Zhang J, Li YY, Qu J, *et al.* SARS-CoV-2 infection in children. N Engl J Med 2020;382:1663-5.
13. Ma YL, Xia SY, Wang M, Zhang SM, DU WH, Chen Q. Clinical features of children with SARS-CoV-2 infection: An analysis of 115 cases. Zhongguo Dang Dai Er Ke Za Zhi 2020;22:290-3.
14. Guo CX, He L, Yin JY, Meng XG, Tan W, Yang GP, *et al.* Epidemiological and clinical features of pediatric COVID-19. BMC Med 2020;18:250.
15. Götzinger F, Santiago-García B, Noguera-Julián A, Lanaspa M, Lancella L, Calò Carducci FI, *et al.* COVID-19 in children and adolescents in Europe: A multinational, multicentre cohort study. Lancet Child Adolesc Health 2020;4:653-61.
16. Garazzino S, Lo Vecchio A, Pierantoni L, Calò Carducci FI, Marchetti F, Meini A, *et al.* Epidemiology, clinical features and prognostic factors of pediatric SARS-CoV-2 infection: Results From an Italian Multicenter Study. Front Pediatr 2021;9:649358.
17. Banerjee S, Guha A, Das A, Nandi M, Mondal R. A preliminary report of COVID-19 in children in India. Indian Pediatr 2020;57:963-4.
18. Sarangi B, Reddy VS, Oswal JS, Malshe N, Patil A, Chakraborty M, *et al.* Epidemiological and clinical characteristics of COVID-19 in Indian children in the initial phase of the pandemic. Indian Pediatr 2020;57:914-7.
19. CDC COVID-19 Response Team. Coronavirus disease 2019 in children – United States, February 12-April 2, 2020. MMWR Morb Mortal Wkly Rep 2020;69:422-6.
20. Han MS, Choi EH, Chang SH, Jin BL, Lee EJ, Kim BN, *et al.* Clinical characteristics and viral RNA detection in children with coronavirus disease 2019 in the Republic of Korea. JAMA Pediatr 2021;175:73-80.
21. Godfred-Cato S, Bryant B, Leung J, Oster ME, Conklin L, Abrams J, *et al.* COVID-19-associated multisystem inflammatory syndrome in children – United States, March-July 2020. MMWR Morb Mortal Wkly Rep 2020;69:1074-80.
22. Jain S, Sen S, Lakshmivenkateshiah S, Bobhate P, Venkatesh S, Udani S, *et al.* Multisystem inflammatory syndrome in children with COVID-19 in Mumbai, India. Indian Pediatr 2020;57:1015-9.
23. Kelvin AA, Halperin S. COVID-19 in children: The link in the transmission chain. Lancet Infect Dis 2020;20:633-4.
24. Sinha I. Guidance for the Clinical Management of Children Admitted Hospital with Proven COVID-19. NHS Foundation Trust. Version-1. Available from: https://alderhey.nhs.uk/application/files/1815/8422/1173/COVID_19_IN_CHILDREN_CLINICAL_GUIDANCE_v1.pdf. [Last accessed on 2020 Apr 14; Last updated on 2020 Mar 13
25. Gupta D, Simalti A, Gupta N, Bhardwaj P, Bandal A, Sachdev A. Management principles of COVID-19 in adolescents & children. Indian J Adolesc Med 2020;2:47-57.
26. Jiehao C, Jin X, Daojiong L, Zhi Y, Lei X, Zhenghai Q, *et al.* A case series of children with 2019 novel coronavirus infection: Clinical and epidemiological features. Clin Infect Dis 2020;71:1547-51.
27. Zimmermann P, Curtis N. COVID-19 in children, pregnancy and neonates: A review of epidemiologic and clinical features. Pediatr Infect Dis J 2020;39:469-77.
28. Hoang A, Chorath K, Moreira A, Evans M, Burmeister-Morton F, Burmeister F, *et al.* COVID-19 in 7780 pediatric patients: A systematic review. EClinicalMedicine 2020;24:100433.
29. Wang Z, Zhou Q, Wang C, Shi Q, Lu S, Ma Y, *et al*. Clinical characteristics of children with COVID-19: A rapid review and meta-analysis. Ann Transl Med 2020;8:620.
30. Bai K, Liu W, Liu C, Fu Y, Hu J, Qin Y, *et al.* Clinical analysis of 25 COVID-19 infections in children. Pediatr Infect Dis J 2020;39:e100-3.
31. Cui X, Zhang T, Zheng J, Zhang J, Si P, Xu Y, *et al.* Children with coronavirus disease 2019: A review of demographic, clinical, laboratory, and imaging features in pediatric patients. J Med Virol 2020;92:1501-10.
32. Yasuhara J, Kuno T, Takagi H, Sumitomo N. Clinical characteristics of COVID-19 in children: A systematic review. Pediatr Pulmonol 2020;55:2565-75.
33. de Souza TH, Nadal JA, Nogueira RJ, Pereira RM, Brandão MB. Clinical manifestations of children with COVID-19: A systematic review. Pediatr Pulmonol 2020;55:1892-9.
34. Patel NA. Pediatric COVID-19: Systematic review of the literature. Am J Otolaryngol 2020;41:102573.