SCOPING REVIEW

Epidemiological, clinical, and radiological comparison of adult and pediatric features in COVID-19: A scoping review

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Abstract

Objective: To assess epidemiological, clinical, and radiological characteristics of the coronavirus disease in children and adults.

Method: The scoping review comprised search on PubMed and Scopus Cochrane databases from January 2020 to April 2021 for English-language articles dealing with clinical and radiological manifestations amongst children and adults affected by coronavirus disease. Two reviewers independently screened the titles and abstracts.

Results: Of the 389 studies initially identified, 39(10%) were reviewed in detail. Data suggested that children were less frequently affected by the coronavirus disease. The affected children showed milder disease with low case fatalities compared to the adults.

Conclusions: There exists significant gaps in knowledge of clinical and radiological aspects of coronavirus disease, but the available scientific data showed that the disease seems to be unusual in children.

Keywords: Children, COVID-19, SARS-CoV2, Epidemiology, Clinical, Radiological.

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Introduction

The novel severe acute respiratory syndrome coronavirus (SARS-CoV-2) was first reported as an epidemic starting from the Hubei province in China. Its rapid spread resulted in it being classified as a Public Health Emergency of International Concern in January 2020. Since then more than 18 million cases of coronavirus disease (COVID-19) have been reported and have contributed to more than 3 million deaths globally.[1] Emergent knowledge suggests that COVID-19 infections are more common in infants and children than was initially anticipated. COVID-19 infections in people aged <18 years have accounted for 8.5% of the total infections. As science regarding the COVID-19 disease and spread continues to change with the advent of new variants, it is crucial to identify the clinical and radiological features of the disease in both adults and children for screening and timely treatment of COVID-19.

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Epidemiological characteristics

It was noted that while all ages were affected by the SARS-CoV-2 virus, the paediatric population aged <18 years contributed approximately 8.5% of the total caseload, with fewer deaths and milder symptoms compared to the adult population.[2] It is, however, possible that the paediatric population is under-reported due to fact that testing is dependent on symptoms and hospitalisations and since children are more likely to be asymptomatic, they are less likely to be tested.[3] Infants and children aged <5 years who are most vulnerable to other respiratory illnesses were incidentally the least affected, contributing only 1.8% to 91 million cases from 101 countries; the mean age for the paediatric population being 6.7 years.[4,5] At the start of the pandemic, children were rarely identified as index cases due to the closure of schools and public spaces, such as parks. However, as restrictions were eased, there have been cases of adolescents being the index cases for family members.[6,7]

The main source of exposure in children has been family contacts which may be due to the fact that schools and public spaces of possible exposure, such as parks, were closed.[3] In adults, the most common transmission occurred either through family members or in close indoor workplace settings; there are frequent cases of clusters resulting from close social contact.[8]

The incubation period varies considerably between children and adults. Adults have been shown to have an average incubation period of 4-5 days whereas the mean number of days of paediatric incubation are 9. This, coupled with the fact that up to 66% of paediatric cases identified were either asymptomatic or had mild symptoms, has clinical significance due to increased infectivity.[9,10]

Methods

The scoping review comprised search on PubMed, Scopus Cochrane and Google Scholar databases from January

2020 to April 2021 for English-language articles dealing with clinical and radiological manifestations amongst children and adults affected by COVID-19. The search included 'coronavirus', 'nCoV', '2019-nCoV', 'SARS-CoV-2' and 'COVID-19'. Studies related to pregnancy, cancer care, infection control practices and other coronavirus-related illnesses, such as the Middle East Respiratory Syndrome (MERS) and SARS were excluded. All the titles and abstracts of the identified studies were evaluated by two reviewers independently. Abstracts not compatible with the eligibility criteria were excluded. After the screening, filter was applied to all the selected studies for retrieving full-text review.

Results and Discussion

Of the 487 studies identified, 439(90.1%) were from PubMed and 48(9.8%) were from Cochrane. After removing the duplicates, 389(88.6%) were shortlisted, and, from among them, 39(10%) were reviewed in detail (Figure-1). In-depth multi-organ system comparison was done for the comparison of clinical characteristics of children and adult with COVID-19 (Table, Figure-2).

Clinical manifestations

Eye: Conjunctival congestion was found in children and adults as an initial symptom or the during the disease.[11-13] The risk factor for congestion can be frequent hand-eye contact in both populations.[11,13] With conjunctival congestion, adults also presented with ocular pain, photophobia and blurred vision.[11]

Respiratory diseases

During the life-threatening pandemic, many children were found to be asymptomatic or were infected as a part

Table: Comparison of clinical characteristics of children and adult with coronavirus disease (COVID-19).

Clinical Manifestations	Paediatrics	Adults
Eye diseases		
Eye manifestation	Among n= 570 children, (48.4%) had conjunctival congestion[12] In 216 patients, 49 children developed ocular symptoms out of which 27 developed conjunctivitis[13]	In a study conducted in Hubei, 12 out 37 patients had conjunctivitis.[57] Conjunctivitis confirmed in 3(2.5) (n=121)[58] 33 (6.2%) patients out of 522 patients had conjunctivitis[11]
Respiratory diseases		
Pharyngitis	In an observational study conducted in china pharyngitis was found in 3% (n= 36) of the patients[14]	33% adults (N=280) were diagnosed with pharyngitis[15]
Bronchopneumonia	In a study of 36,Pneumonia was present in 19(52%)[14] 27%(n= 41) children presented with pneumonia[16] One child (11.1%) among 9 children[17]	71.4% (n=14) had pneumonia[26] All patients 100% (n=41) had pneumonia[28] All 100%(138)of the patients developed pneumonia[19]
ARDS	13(0·6%) children developed ARDS (n=2143)[23]	A study conducted in China showed 25% of the patient had ARDS out of 187[21] A cohort n= 201, 84 patients (41.8%) patients developed ARDS,[22] 29% of the patient developed ARDS[20] 19.6% had ARDS[19]
Gastrointestinal diseases		
Gastritis/ gastroenteritis	Among 41 children 5% had gastroenteritis[16] Among n=570, (90.9%) had gastrointestinal symptoms[12]	A cross sectional study 1% of the adult had gastroenteritis[25] In 59 patients with COVID 19, 15(26%) of the patients had gastritis[59,12] Among 204 patients 35(34%) had gastritis[25]
Viral hepatitis	Among 44 children 19 develop viral Hepatitis (43%)	10.5%(1099) patient had increased bilirubin levels[60] 19 (15%) had acute hepatitis out of 183 patients[21]
Cardio Vascular diseases		
Acute Myocardial Infarction	Six children had increased CK MB (86.5%) n=570[12]	37.50% (6 of 16) n=187 with high troponin levels and without underlying CVS disease[21] 5 out of 41 patients had MI associated with COVID 19[24] 7.2% out of 138 patients had MI[19]
Acute Kidney Injury	Among 570 children, 18.4% of the children acute kidney injury[12]	14.6% (n=187) developed acute kidney injury[21] (9 of 198 [4.5%]) diagnosed on the basis of high plasma urea and creatinine[14]
Encephalopathy	N=50, 4 patients (14.8%) had neurological symptoms[26]	N= 214, 76 (36%) patients had neurological symptoms which included acute cerebrovascular disease, ataxia and skeletal muscle injury[61]
Skin manifestation	dermatologic or mucocutaneous lesions were seen in 70.9% n=570[12]	N= 88, 18 (20.4%) patients' erythematous rash (14 patients), widespread urticaria (three patients) and chickenpox-like vesicles (one patient).
Radiological Findings:		
	Peri-bronchial distribution was seen more frequently in paediatric group, as compared to adult group (28.6% versus 2.3%, p = 0.048) while sub-pleural distribution was seen almost equally in both the groups[45]	Multifocal bilateral ground glass opacities (GGOs) with patchy consolidations, prominent peripheral distribution and preferred posterior part or lower lobe predominance[36-38]

ARDS: Acute respiratory distress syndrome, CNS: Central nervous system.

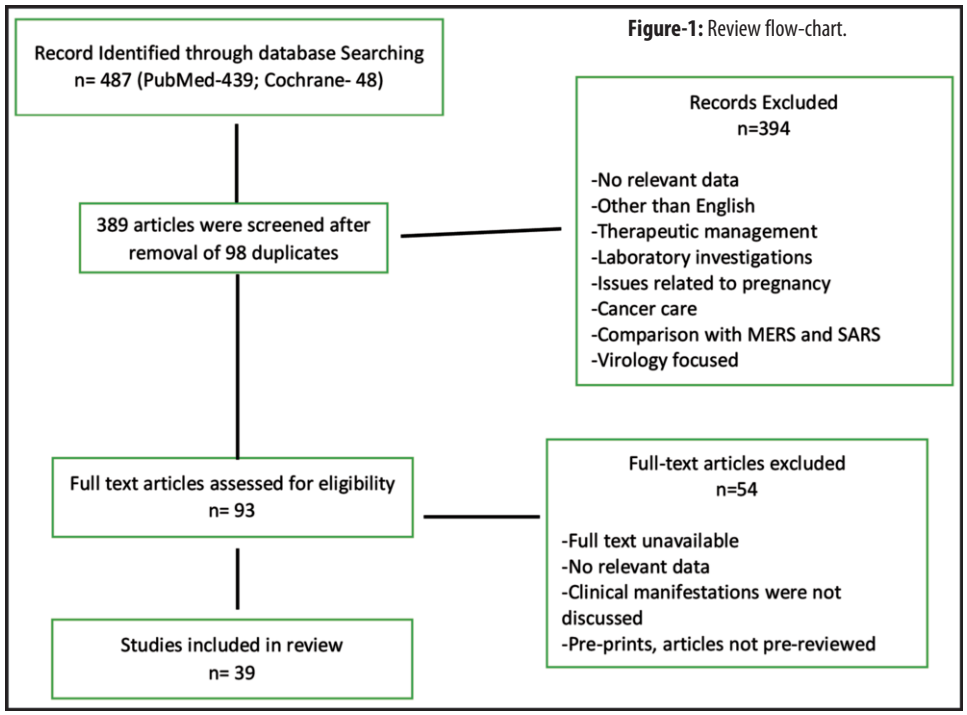

Figure-1: Review flow-chart.

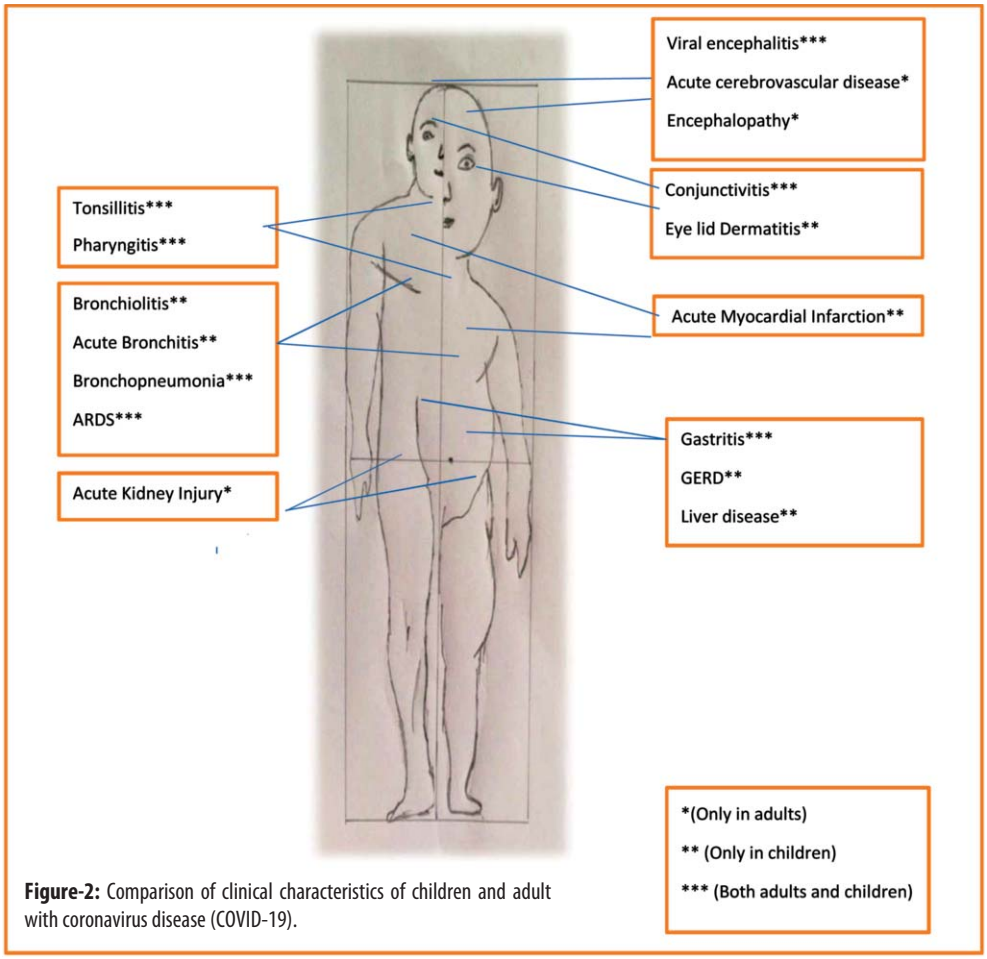

Figure-2: Comparison of clinical characteristics of children and adult with coronavirus disease (COVID-19).

of family clusters. They were mostly asymptomatic or had milder respiratory disease.

Pharyngitis: In an observational study, conducted in China on children aged from 0 months to 16 years, 3% (n=36) had pharyngitis.[14] In another study conducted in France, 33% adults (n=280) were diagnosed with pharyngitis.[15]

Bronchiolitis: A study from Spain conducted on children aged 9 months to 6 years, 12% (n=41) were identified as having bronchiolitis.[16]

Acute bronchitis: A retrospective review identified that among children (n=9; aged 2-9 years) with their 14 adult family members, 2 had bronchitis, but none of the adults reported it.[17]

Pneumonia: An observational study conducted on children (n=36; aged from 0 months to 16 years) in China, 19(52%) presented with pneumonia.[14] However, in another study, a child with 10 adult family members was identified with pneumonia.[17] Similarly, a study from Spain showed 11 children (age: 9 months to 6 years; n=41) had pneumonia.[16] Moreover, two studies conducted in Wuhan, China, all adults presented with pneumonia.[17,18]

Acute respiratory distress syndrome: A study conducted in China had 138 patients of whom 19.6% (n=27) developed Acute respiratory distress syndrome (ARDS).[19] A study in China showed the presence of ARDS in 12 (29%) of 41 patients as a complication of SARS-CoV-2.[20] Another study in China showed 25% of the patients

had ARDS out of 187.[21] A cohort of 84 patients was enrolled in a study which reported 41.8% patients with ARDS.[22] Moreover, a study on children showed that 13(0·6%) children developed ARDS (n=2143).[23]

Acute myocardial injury: A study analysed prospectively collected data of 41 hospitalised patients. In 5(12%) patients, there was a substantial raise in troponin I levels, , showing evidence of acute myocardial injury (AMI). There was no prior history of cardiac disease among these patients.[24] A retrospective review was conducted on 9 children aged 2-9 years and their 14 adult family members admitted to a hospital in China. It was reported that 6 children and 2 adults had high creatine kinase-myocardial band (CK-MB), which means that SARS-CoV-2 can cause heart injury; CK-MB was taken as an indicator of myocardial injury.[9] Another study reported that among 187 patients, 52 had elevated troponin I. Underlying cardiovascular disease (CVD) was present in 36 (54%) patients, whereas 16(46%) had high troponin I without any underling disease.[21] From other recent data, among 138 hospitalised patients, 16.7% had arrhythmias and 7.2% had AMI. Cardiac injury was considered present if the serum levels of cardiac biomarkers, like troponin I, were above the 99th percentile upper reference limit, or new abnormalities were shown in electrocardiography and echocardiography.[19]

Gastrointestinal system: In a multi-centre cross-sectional study, 103(50.5%) of 204 patients presented with one or more digestive symptoms. The symptoms included lack of appetite (78%), diarrhoea (34%), vomiting (3.9%), and abdominal pain (1.9%). Only 1% patients were diagnosed having gastroenteritis, oesophageal reflux disease (GERD), hepatic insufficiency and fatty liver. Moreover, increased levels of alanine transaminase (ALT) and aspartate aminotransferase (AST) were significantly high in patients suffering from digestive symptoms compared to the patients without the digestive symptoms. Therefore, it was suggested that the patient suffering from digestive illness are more prone to develop liver injury.[25] On the contrary, a study in Spain showed that only 5% children had gastroenteritis.[16]

Viral hepatitis: A retrospective single-centre case series analysed patients with COVID-19 at the Seventh Hospital of Wuhan City, and revealed that among 187 patients, 19(15%) developed acute liver injury as a complication of COVID-19.[21] In another retrospective cohort study, liver injury was found in 43(22%) patients with increased ALT and 59(30%) patients with increased AST.[26] Furthermore, case report of 59-year-old women who presented in the emergency department with the complaint of dark-coloured urine, work-up done for acute hepatitis revealed that AST and ALT were very high. On next day, she developed respiratory complaints and was found to be positive for COVID-19.[27]

Acute kidney injury: A retrospective study in China had 187 patients, and, of them, 18(15%) patients suffered acute renal injury as a complication of SARS-CoV-2.[21] Also, 9(4.5%) patients each had kidney injury indicated by elevated plasma urea and serum creatinine.[26]

Viral encephalitis: A case report of a 24-year-old male with history of fever and generalised fatigue for nine days, brain magnetic resonance imaging (MRI) showed hyper-intensity along the wall of the right lateral ventricle and hyper-intense signal changes in the right mesial temporal lobe and hippocampus, suggesting the possibility of SARS-CoV-2 meningitis.[20] Another case report of an 11-year-old previously healthy child who presented with status epilepticus, cerebrospinal fluid (CSF) revealed encephalitis.[19]

Acute cerebrovascular disease: The four patients reported with COVID-19 in the city of Sakarya, Turkey were simultaneously diagnosed with acute ischaemic stroke. All four patients had risk for stroke, and three of them had hypertension and 1 had diabetes mellitus. Of the patients with stroke, 2 had large vessel stenosis, and 2 had small vessel occlusion.[28]

Skin Manifestation: The cutaneous manifestation of SARS-CoV-2 infection in children differ from those in adults. In paediatrics, the chilblain-like lesions is more common, and these erythematous, oedematous macules are found in the dorsum of the fingers and toes.[29] Chilblains-like lesions were reported from France, the Middle East and Spain.[30-32] In adults, the presence of erythematous rash, urticaria and chicken-pox-like vesicles that mainly appear on the trunk, are less itchy and heal in a few days.[33-35]

Radiological finding

Radiological investigations have an established role in the early detection and management of COVID-19. Thin slice chest computed tomography (CT) is the radiological investigation of choice because of its proven role in the early detection of abnormal findings associated with COVID-19. Chest radiography has also got some utility, but has lower sensitivity compared to CT, and that is why it is not used as first-line imaging modality for COVID-19.[36,37] Much has been written about radiological presentation of COVID-19 in adult patients compared to paediatrics because of lower number of cases in the paediatric population. Chest CT findings are varied; some may be specific and others non-specific based on the

published literature. The findings consistently reported in literature regarding the imaging appearance of COVID-19 in adults are multifocal bilateral ground glass opacities (GGOs) with patchy consolidations, prominent peripheral distribution and preferred posterior part or lower lobe predominance.[38-40] GGOs with typical crazy-paving pattern have also been described. Consolidations as solitary and pure findings have been reported much less commonly.[37,41] The reversed halo sign (central GGO surrounded by a more or less complete ring of consolidation) on CT examination has also been observed associated with COVID-19.[37,42]

On the other hand, pleural effusion, lung cavitation and lymphadenopathy have also been reported with rare occurrence.[41,43-45] Pneumothorax has also been reported in a case report.[46] According to a recent study focussing on the differences in clinical and imaging presentation of paediatric patients in comparison with adult patients, CT chest was more likely positive in adults (91.5%) compared to paediatric patients (50%). It has also been reported that SARS-CoV-2 involved greater number of pulmonary lobes in adults compared to the paediatric population, meaning widespread occurrence of pulmonary opacities on CT in adults. Bilateral lung involvement was seen more frequently in adults compared to paediatric patients (83.7% versus 57.1%). Peri-bronchial distribution was seen more frequently in the paediatric group compared to the adult group (28.6% versus 2.3%, p = 0.048), while sub-pleural distribution was seen almost equally in both the groups. GGO was the most common feature (53.5%), followed in frequency by GGO with consolidations in adults. In the paediatric group, GGO (42.9%) was also the common feature followed in frequency by bronchial wall thickening (28.6%), GGO with consolidations (14.3%) and nodules (14.3%). Lung severity scores in adults were higher than those in the paediatric group (8.89±4.54 versus 1.86±2.41).[47]

A study done in China reported two types of radiological findings in a cohort of 36 children: multiple opacities and patchy opacities. More than half of them (53%) had pulmonary GGOs on CT scan, consistent with findings recorded in the adults. Approximately half of them had no abnormal radiological findings.[14] Another study recorded radiological findings in 9 COVID-19 children and their 14 positive family members. Five of the 9 children (55%) had no abnormal findings on chest radiograph. In the remaining 4 children, 2 had findings consistent with bronchitis, 1 showed bronchopneumonia and 1 had pulmonary consolidation associated with GGO. On the other hand, only 4(28.6%) of the adult patients had normal chest radiographs. In those having abnormal chest radiographs, pulmonary consolidation, nodular shadows and GGOs were seen in 50%, 42.9% and 35.7% respectively.[17]

A letter published in the 'New England Journal of Medicine' recorded clinical and radiological findings of 171 COVID-19 children. Out of these, 111 were diagnosed with pneumonia. Those having pneumonia, GGOs, local patchy shadowing, bilateral patchy shadowing and interstitial abnormalities were seen in 32.7%, 18.7%, 12.3% and 1.2% children respectively.[48] One study recorded findings in three neonates with COVID-19 born to mothers with COVID-19. All the three had non-specific findings on chest radiographs.[49] Chest CT findings in 15 paediatric patients with COVID-19 in another study found that 6 of them had no clear lesions, while 9 children had either symmetrical or asymmetrical sub-pleural ground glass nodular shadowing involving single or multiple lobes.[50]

Another study documented CT chest findings in 20 paediatric COVID-19 patients in early, advanced, critical and recovery stages. Four children (20%) had no pulmonary lesions, while 6 (30%) had unilateral and 10 (50%) had bilateral pulmonary lesions in the early stage. All the sixteen children showed sub-pleural lesions consistent with imaging appearance of COVID-19 in adults. Ten patients showed consolidation with surrounding halo sign, while GGOs, fine mesh shadowing and tiny nodules were seen in 12, 4 and 3 patients respectively. Children in advanced and critical stages had further involvement of the pulmonary parenchyma with expansion in the lesions and densities. Six patients (6/20) underwent CT chest examination in the recovery phase. There was complete resolution of pulmonary lesions in two cases, while the rest had some non-residual findings.[51] One study analysed 31 paediatric patients diagnosed with COVID-19 in northern China. Out of these, 30 cases had CT chest examination and one underwent chest X-ray examination. Out of 30 CT chest examinations, 16(53%) had no abnormal findings, while 14 (47%) had abnormal findings. Nine of those having abnormal Chest CT examinations, had sub-pleural patchy ground glass shadows and nodules, and some were associated with consolidations. None of the children had findings of white lung, pleural or pneumothorax.[52] Few case series featuring COVID-19 patients found that 50% to 80% of the children had abnormal findings on CT chest, predominantly sub-pleural GGOs and nodules in lower lobes.[53-55]

In the light of literature, children tend to have repeated viral exposures which might help their immune system to be stronger against SARS-CoV-2.[5] Moreover, higher

concentration of angiotensin converting enzyme-2 in children can also be responsible for milder disease in children.[56]

Conclusion

COVID-19 has a variety of clinical presentations in children as well as in adults, and fever and respiratory symptoms alone should not be considered a hallmark. Children and adults both have almost similar symptoms. However, the course of disease is generally milder in children, indicating better prognosis compared to adults.

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References

1. Organization WH. WHO Coronavirus (COVID-19) Dashboard 2021 [Available from: https://covid19.who.int. [Accessed 1st June, 2021]
2. Organization WH. Coronavirus disease (COVID-19): Schools 2020 [Available from: https://www.who.int/news-room/q-a-detail/coronavirus-disease-covid-19-schools. [Accessed 1st June, 2021]
3. Warner S, Richter A, Stamataki Z, Kelly D. Understanding COVID-19: are children the key? BMJ Paediatrics Open. 2021;5(1):e001063.
4. hub Ud. COVID-19 and children 2020 [Available from: https://data.unicef.org/covid-19-and-children/.[Accessed 1st June, 2021]
5. Ludvigsson JF. Systematic review of COVID?19 in children shows milder cases and a better prognosis than adults. Acta paediatrica. 2020;109(6):1088-95.
6. Prevention CoDCa. Science Brief: Transmission of SARS-CoV-2 in K-12 Schools and Early Care and Education Programs - Updated 2021 [Available from: https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/transmission_k_12_schools.html. [Accessed 1st June, 2021]
7. Goldstein E, Lipsitch M, Cevik M. On the Effect of Age on the Transmission of SARS-CoV-2 in Households, Schools, and the Community. The Journal of infectious diseases. 2021;223(3):362-9.
8. McIntosh K, Hirsch M, Bloom A. Coronavirus disease 2019 (COVID-19): Epidemiology, virology, and prevention. Lancet Infect Dis. 2020;1:2019-20.
9. Guo C-X, He L, Yin J-Y, Meng X-G, Tan W, Yang G-P, et al. Epidemiological and clinical features of pediatric COVID-19. BMC medicine. 2020;18(1):1-7.
10. Li B, Zhang S, Zhang R, Chen X, Wang Y, Zhu C. Epidemiological and clinical characteristics of COVID-19 in children: a systematic review and meta-analysis. Frontiers in pediatrics. 2020;8:709.
11. Chen L, Deng C, Chen X, Zhang X, Chen B, Yu H, et al. Ocular manifestations and clinical characteristics of 535 cases of COVID?19 in Wuhan, China: a cross?sectional study. Acta Ophthalmologica. 2020;98(8):e951-e9.
12. 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. Morbidity and Mortality Weekly Report. 2020;69(32):1074.
13. Ma N, Li P, Wang X, Yu Y, Tan X, Chen P, et al. Ocular manifestations and clinical characteristics of children with laboratory-confirmed COVID-19 in Wuhan, China. JAMA ophthalmology. 2020;138(10):1079-86.
14. Qiu H, Wu J, Hong L, Luo Y, Song Q, Chen D. Clinical and epidemiological features of 36 children with coronavirus disease 2019 (COVID-19) in Zhejiang, China: an observational cohort study. The Lancet Infectious Diseases. 2020.
15. Amrane S, Tissot-Dupont H, Doudier B, Eldin C, Hocquart M, Mailhe M, et al. Rapid viral diagnosis and ambulatory management of suspected COVID-19 cases presenting at the infectious diseases referral hospital in Marseille, France,-January 31st to March 1st, 2020: A respiratory virus snapshot. Travel medicine and infectious disease. 2020:101632.
16. Tagarro A, Epalza C, Santos M, Sanz-Santaeufemia FJ, Otheo E, Moraleda C, et al. Screening and severity of coronavirus disease 2019 (COVID-19) in children in Madrid, Spain. JAMA pediatrics. 2020.
17. Su L, Ma X, Yu H, Zhang Z, Bian P, Han Y, et al. The different clinical characteristics of corona virus disease cases between children and their families in China-the character of children with COVID-19. Emerging microbes & infections. 2020;9(1):707-13.
18. Tagarro A, Epalza C, Santos M, Sanz-Santaeufemia FJ, Otheo E, Moraleda C, et al. Screening and severity of coronavirus disease 2019 (COVID-19) in children in Madrid, Spain. JAMA pediatrics. 2021;175(3):316-7.
19. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. Jama. 2020;323(11):1061-9.
20. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The Lancet. 2020;395(10223):497-506.
21. Guo T, Fan Y, Chen M, Wu X, Zhang L, He T, et al. Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19). JAMA cardiology. 2020.
22. Wu C, Chen X, Cai Y, Zhou X, Xu S, Huang H, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA internal medicine. 2020.
23. Sinha IP, Harwood R, Semple MG, Hawcutt DB, Thursfield R, Narayan O, et al. COVID-19 infection in children. The Lancet Respiratory Medicine. 2020.
24. Zheng Y-Y, Ma Y-T, Zhang J-Y, Xie X. COVID-19 and the cardiovascular system. Nature Reviews Cardiology. 2020;17(5):259-60.
25. Pan L, Mu M, Yang P, Sun Y, Wang R, Yan J, et al. Clinical characteristics of COVID-19 patients with digestive symptoms in Hubei, China: a descriptive, cross-sectional, multicenter study. The American journal of gastroenterology. 2020;115.
26. Abdel-Mannan O, Eyre M, Löbel U, Bamford A, Eltze C, Hameed B, et al. Neurologic and radiographic findings associated with COVID-19 infection in children. JAMA neurology. 2020;77(11):1440-5.
27. Wander P, Epstein M, Bernstein D. COVID-19 Presenting as Acute Hepatitis. The American journal of gastroenterology. 2020.
28. Abdulkadir T, Ünlüba? Y, Alemdar M, Akyüz E. Coexistence of COVID-19 and acute ischemic stroke report of four cases. Journal of Clinical Neuroscience. 2020;77:227-9.
29. Andina D, Belloni?Fortina A, Bodemer C, Bonifazi E, Chiriac A, Colmenero I, et al. Skin manifestations of COVID?19 in children: part 1. Clinical and experimental dermatology. 2021;46(3):444-50.
30. Khalili M, Iranmanesh B, Mohammadi S, Aflatoonian M. Cutaneous and histopathological features of coronavirus disease 2019 in pediatrics: A review article. Dermatologic Therapy. 2021;34(1):e14554.
31. Alramthan A, Aldaraji W. Two cases of COVID?19 presenting with a clinical picture resembling chilblains: first report from the

Middle East. Clinical and experimental dermatology. 2020.
32. Romaní J, Baselga E, Mitjà O, Riera-Martí N, Garbayo P, Vicente A, et al. Chilblain and acral purpuric lesions in Spain during COVID confinement: retrospective analysis of 12 cases. Actas dermo-sifiliograficas. 2020;111(5):426.
33. Recalcati S. Cutaneous manifestations in COVID-19: a first perspective. J Eur Acad Dermatol Venereol. 2020;34(5).
34. Bouaziz J, Duong T, Jachiet M, Velter C, Lestang P, Cassius C, et al. Vascular skin symptoms in COVID-19: a french observational study. J Eur Acad Dermatol Venereol. 2020;34(9):e451-e2.
35. Mahé A, Birckel E, Krieger S, Merklen C, Bottlaender L. A distinctive skin rash associated with coronavirus disease 2019? Journal of the European Academy of Dermatology and Venereology. 2020.
36. Chan JF-W, Yuan S, Kok K-H, To KK-W, Chu H, Yang J, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. The Lancet. 2020;395(10223):514-23.
37. Ng M-Y, Lee EY, Yang J, Yang F, Li X, Wang H, et al. Imaging profile of the COVID-19 infection: radiologic findings and literature review. Radiology: Cardiothoracic Imaging. 2020;2(1):e200034.
38. Kanne JP. Chest CT findings in 2019 novel coronavirus (2019-nCoV) infections from Wuhan, China: key points for the radiologist. Radiological Society of North America; 2020.
39. Kim H. Outbreak of novel coronavirus (COVID-19): What is the role of radiologists? : Springer; 2020.
40. Lee KS. Pneumonia associated with 2019 novel coronavirus: can computed tomographic findings help predict the prognosis of the disease? Korean Journal of Radiology. 2020;21(3):257-8.
41. Pan F, Ye T, Sun P, Gui S, Liang B, Li L, et al. Time course of lung changes on chest CT during recovery from 2019 novel coronavirus (COVID-19) pneumonia. Radiology. 2020:200370.
42. Kong W, Agarwal PP. Chest imaging appearance of COVID-19 infection. Radiology: Cardiothoracic Imaging. 2020;2(1):e200028.
43. Chung M, Bernheim A, Mei X, Zhang N, Huang M, Zeng X, et al. CT imaging features of 2019 novel coronavirus (2019-nCoV). Radiology. 2020;295(1):202-7.
44. Pan Y, Guan H, Zhou S, Wang Y, Li Q, Zhu T, et al. Initial CT findings and temporal changes in patients with the novel coronavirus pneumonia (2019-nCoV): a study of 63 patients in Wuhan, China. European radiology. 2020:1-4.
45. Liu T, Huang P, Liu H, Huang L, Lei M, Xu W, et al. Spectrum of chest CT findings in a familial cluster of COVID-19 infection. Radiology: Cardiothoracic Imaging. 2020;2(1):e200025.
46. Sun R, Liu H, Wang X. Mediastinal emphysema, giant bulla, and pneumothorax developed during the course of COVID-19 pneumonia. Korean Journal of Radiology. 2020;21(5):541.
47. Chen A, Huang J, Liao Y, Liu Z, Chen D, Yang C, et al. Differences in clinical and imaging presentation of pediatric patients with COVID-19 in comparison with adults. Radiology: Cardiothoracic Imaging. 2020;2(2):e200117.
48. Lu X, Zhang L, Du H, Zhang J, Li YY, Qu J, et al. SARS-CoV-2 infection in children. New England Journal of Medicine. 2020;382(17):1663-5.
49. Zeng L, Xia S, Yuan W, Yan K, Xiao F, Shao J, et al. Neonatal early-onset infection with SARS-CoV-2 in 33 neonates born to mothers with COVID-19 in Wuhan, China. JAMA pediatrics. 2020.
50. Feng K, Yun Y, Wang X, Yang G, Zheng Y, Lin C, et al. Analysis of CT features of 15 children with 2019 novel coronavirus infection. Zhonghua er ke za zhi= Chinese journal of pediatrics. 2020;58:E007-E.
51. Xia W, Shao J, Guo Y, Peng X, Li Z, Hu D. Clinical and CT features in pediatric patients with COVID?19 infection: Different points from adults. Pediatric pulmonology. 2020;55(5):1169-74.
52. Wang D, Ju X, Xie F, Lu Y, Li F, Huang H, et al. Clinical analysis of 31 cases of 2019 novel coronavirus infection in children from six provinces (autonomous region) of northern China. Zhonghua er ke za zhi= Chinese journal of pediatrics. 2020;58(4):E011-E.
53. Hu Z, Song C, Xu C, Jin G, Chen Y, Xu X, et al. Clinical characteristics of 24 asymptomatic infections with COVID-19 screened among close contacts in Nanjing, China. Science China Life Sciences. 2020:1-6.
54. Cao Q, Chen Y-C, Chen C-L, Chiu C-H. SARS-CoV-2 infection in children: Transmission dynamics and clinical characteristics. Journal of the Formosan Medical Association. 2020;119(3):670.
55. Wang Y, Wang Y, Chen Y, Qin Q. Unique epidemiological and clinical features of the emerging 2019 novel coronavirus pneumonia (COVID?19) implicate special control measures. Journal of medical virology. 2020;92(6):568-76.
56. Cristiani L, Mancino E, Matera L, Nenna R, Pierangeli A, Scagnolari C, et al. Will children reveal their secret? The coronavirus dilemma. Eur Respiratory Soc; 2020.