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Children with Coronavirus Disease 2019 (COVID-19): A Review of Demographic, Clinical, Laboratory and Imaging Features in 2,597 Pediatric Patients

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Abstract: An epidemic of coronavirus disease 2019 (COVID-19) has been spreading worldwide. With the rapid increase in the number of infections, children with COVID-19 appear to be rising. Most research findings regarding adult cases, which are not always transferrable to children. Evidence-based studies are still expected to formulate clinical decisions for pediatric patients. In this review, we evaluated the demographic, clinical, laboratory and imaging features from 2,597 pediatric patients of COVID-19 that reported recently. We found that even lymphopenia was the most common lab finding in adults, it infrequently occurred in children (9.8%). Moreover, elevated creatine kinase MB isoenzyme (CK-MB) was much more commonly observed in children (27.0%) than that in adults, suggesting that heart injury would be more likely to happen in pediatric patients. Our analysis may contribute to determine the spectrum of disease in children, as well as to develop strategies to control the disease transmission.

Highlights: An epidemic of COVID-19 has been spreading worldwide. Most research findings regarding adult cases, which are not always transferrable to children. Here, we collect 2,597 pediatric patients and summarize the demographic, clinical, laboratory and imaging characteristic of children with COVID-19.

Keywords: COVID-19; SARS-CoV-2; 2019-nCoV; Children; Pediatric Patients

1. Introduction

In December 2019, a cluster of patients with pneumonia were epidemiologically linked to a seafood wholesale market in Wuhan, China. A previously unknown betacoronavirus (initially named 2019-nCoV) was discovered from bronchoalveolar-lavage fluid (BALF) samples of these patients[1-3]. As of Jan 30, 2020, 7736 cases infected with this novel coronavirus had been confirmed in China, and 98 cases had also been cumulatively reported from 18 countries outside China [4], which prompted the World Health Organization (WHO) declared this new coronavirus outbreak as a global health emergency[5]. On Feb 11, 2020, WHO named the illness associated with 2019-nCoV as coronavirus disease 2019 (COVID-19)[6].On the same day, Coronavirus Study Group (CSG) of the International Committee on Taxonomy of Viruses designated 2019-nCoV as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). On Mar 11, 2020, WHO classified COVID-19 as a pandemic as the rapid worldwide spread of SARS-CoV-2. Until Mar 30, 2020, WHO reported 693,224 confirmed cases, including 33,106 deaths all over the world[7]. Reported illnesses have ranged from mild symptoms to severe illness for COVID-19 cases. In most pediatric patients, SARS-CoV-2 causes mild or moderate symptoms, which can include fever and cough. Contrarily, the risk is statistically greater for older adults and people with other health problems. Nevertheless, a letter published in *the New England Journal of Medicine* by Lu *et al.* reported the death of a 10-month-old child with COVID-19. This infant had intussusception and multiorgan failure and died 4 weeks after admission[8]. Another study published on *Pediatrics* by Dong and co-authors recently examined 731 confirmed and 1,412 suspected cases of children with COVID-19, which explored that children infected with novel coronavirus showed less severe symptoms than adults, though infants and toddlers were vulnerable to moderate and severe infection[9]. This study noted one death of a 14-year-old child with COVID-19, and found 5.9% of cases were severe, compared with 18.5% of adults experiencing severe

symptoms[10]. Given the above cases, the induction factor for the discrepancy of clinical manifestations among children and adults remains to be determined. In this review, we collected 2,597 pediatric patients with COVID-19, included 1,185 confirmed and 1,412 suspected cases that reported recently. Based on analysis of demographic, clinical, laboratory and imaging characteristics, to help understanding the natural history of COVID-19 transmission in children, that would otherwise contribute to limit the threat of this human pandemic.

2. Demographic Characteristics and Illness Severity of COVID-19 in Children

A total of 2,597 cases of children with COVID-19 from 24 articles were collected[8,9,11-32], including 1,185 confirmed cases and 1,412 suspected cases (Table 1). The COVID-19 cases were confirmed with positive SARS-CoV-2 nucleic acid in nasal and pharyngeal swab specimens or blood samples. While if a child had negative result of SARS-CoV-2 RNA test, but had any two of abnormal conditions in clinical symptoms, laboratory tests and chest X-ray imaging, was defined as suspected case[9]. Meanwhile, all the suspected children had exposed to COVID-19 patients within the last two weeks[9]. All children had completed the vaccines recommended by the childhood immunization program. Among them, age information was available from 2,517 cases. Most of them (2,492 cases) followed the age distribution as: <1 year: 446 (17.9%); 1–5 years: 593 (23.8%); 6–10 years: 626 (25.1%); 11–15 years: 492 (19.7%); >15years: 335 (13.4%). Age distribution of another 25 cases was grouped by using different criteria[32], related information was presented in Table 1. Gender information was available from 2,566 cases, and the male/female ratio was 1453/1113 (Table 1).

The illness severity of COVID-19 was defined based on the clinical characteristics, laboratory testing results and chest radiographs, including asymptomatic infection, mild, moderate, severe and critical[9]. According to our analysis of the 2,597 cases (Table 1), 198 were asymptomatic infection (7.6%), 1,181 were mild (45.5%), 1,079 were moderate (41.5%), 113 were severe (4.4%), 23 were critical (0.9%) and 3 were death (0.1%). Among them, 2,558 children (98.5%) have an epidemiological link to the adult patients or an exposure to Wuhan or other epidemic areas. We also summarized the incubation period of 18 cases collected from 7 articles. 16 (88.9%) of them showed symptoms within 2 to 10 days of exposure[14,20,22,23,27], while the symptom onset occurred within 19 days[25] and 24 days[21] respectively for another two cases (11.1%).

3. Clinical Characteristics of COVID-19 in Children

The clinical information from 452 children with COVID-19 in 23 articles were collected and analyzed (Table 2). Even though the signs and symptoms were presented in variety, over the course of disease, most children with COVID-19 experienced the following: fever (195/452, 43.1%), cough (196/452, 43.4%), sore throat (92/452, 20.4%), tachycardia (76/452, 16.8%), rhinorrhea (74/452, 16.4%), nasal congestion (69/452, 15.3%), tachypnea/shortness of breath (57/452, 12.6%), diarrhea (30/452, 6.6%), vomiting (26/452, 5.8%), myalgias or fatigue (23/452, 5.1%), hypoxemia (8/452, 1.8%), chest pain (2/452, 0.4%). Among 23 critical cases, six of them (6/23, 26.1%) were complicated with underlying diseases: one case of 1-year-old boy with renal calculi and

hydronephrosis; one case of 8-year-old boy with acute lymphoblastic leukemia and myelosuppression after chemotherapy; one case of 11-month-old boy with intussusception[11]; one case of 8-month-old boy with congenital heart diseases, malnutrition, suspected hereditary metabolic diseases; one case of 1-year-old boy with congenital heart diseases[32]; and the last one was premature infants with acute respiratory distress syndrome (ARDS)[29]. It was reported that the first severe COVID-19 child in China, who started with gastrointestinal symptoms, and unobvious early respiratory symptoms, then progressed to ARDS, septic shock and acute renal failure rapidly, even there was no underlying diseases[31]. The clinical manifestations of neonates were atypical. For the 5 cases, 3 of them (60%) had fever and vomiting, 2 of them (40%) had diarrhea and 1 of them (20%) had cough[24,26,29].

4. Laboratory Characteristics of COVID-19 in Children

Laboratory indicators were available from 445 children with COVID-19 in 22 articles (Table 3), and the primary parameters were generalized. Blood routine: leukocytes was normal in 186 cases (186/249, 74.7%); leukocytosis in 22 cases (22/249, 8.8%); leukopenia in 88 cases (88/420, 21%) and lymphopenia in 42 cases (42/430, 9.8%). Inflammatory markers: procalcitonin (PCT) increased in 111 cases (111/272, 40.8%); C-reactive protein (CRP) increased in 54 cases (54/287, 18.8%); lactate dehydrogenase (LDH) increased in 20 cases (20/98, 20.4%). Liver function: alanine aminotransferase (ALT) increased in 42 cases (42/376, 11.2%); aspartate aminotransferase (AST) increased in 43 cases (43/249, 17.3%). Renal function: blood creatinine increased in 2 case (2/91, 2.2%) and urea nitrogen increased in 1 case (1/66, 1.5%)[31,32]. Myocardial enzyme detection: creatine kinase (CK) increased in 5 cases (5/47, 10.6%); creatine kinase MB isoenzyme (CK-MB) increased in 53 cases (53/196, 27.0%). Blood coagulation function: D-dimer increased in 33 cases (33/272, 12.1%). One of the above studies showed that in 115 pediatric patients, the elevated ALT and CK-MB mainly concentrated in infantile children, suggesting that the younger children are more likely to present higher levels of ALT and CK-MB[11].

5. Imaging Characteristics of COVID-19 in Children

Computed tomography (CT) screening was recommended for COVID-19 diagnosis in China. Lung CT information was available from 409 children with COVID-19 in 21 articles (Table 4). Thereinto, 178 cases (43.5%) had no obvious abnormality, 231 cases (56.5%) had inflammatory lesions of lung, including 2 cases (2/409, 0.5%) of white lung and 3 cases (3/409, 0.7%) of pleural effusion (Table 4). Furthermore, pulmonary imaging data from 294 cases were classified in 20 articles (Table 4): 87 (87/294, 29.6%) cases with ground glass opacities, 60 (60/294, 20.4%) with local patchy shadow, 43 (43/294, 14.6%) with bilateral patchy shadow, and 2 (2/294, 0.7%) with interstitial lesions. One article reported that 47 cases (47/115) of lung CT showed ground glass opacities, fibrous cord shadows, patchy lesions and pulmonary consolidation, but there was no specific classification[11]. After active treatment, pulmonary imaging lesions were absorbed to varying degrees (3-5 days). Severe children may have multiple lobar lesions of both lungs and white lung[11], which indicated that the inflammatory reaction is serious. The chest X-

ray or CT manifestations of infants (17d, 3, 6, 9 months old) are not typical, and its mechanism is worth further study[13,21,26].

6. Nucleic Acid Testing of SARS-CoV-2 RNA in Children with COVID-19

In the total of 2,597 cases from 24 articles, 1,185 children with confirmed COVID-19 were diagnosed by testing SARS-CoV-2 nucleic acid with reverse transcription polymerase chain reaction (RT-PCR) from nasopharyngeal secretions or sputum samples. After analyzing the 731 confirmed cases[9], Dong and co-authors proposed that the median time from symptom onset to SARS-CoV-2 positive was 2 days (0-42 days) (Table 5). Meanwhile, some other studies also concluded that the time to diagnostic of SARS-CoV-2 infection was mainly ranged within 1-5 days, but cannot excluded longer time for some unexpected cases (Table 5). The duration time of SARS-CoV-2 shedding would differ in different specimens. It was demonstrated that SARS-CoV-2 RNA could be detected from nasopharyngeal/throat swabs for 3-23 days after illness onset. Extended time was reported in fecal samples, as the viral RNA could persist as long as 43 days in stools (Table 5).

7. Drug Treatment Options for Children with COVID-19

Once confirmed COVID-19 in children, treatment in designated hospital would be recommended, as childhood infections were mainly caused by family clustering outbreaks and

rapid deterioration. Treatment related information was available from 309 children with COVID-19 in 17 articles[8,12-14,16,17,19-21,23-25,27-29,31,32], all of which had supportive treatment and interferon atomization. 37 cases were treated with lopinavir/ritonavir, 8 cases were treated with oseltamivir, 6 cases were treated with ribavirin, 22 cases were treated with oral Chinese medicine, 28 cases received empirical antibiotic therapy. 8 children were admitted to the intensive care unit (ICU), 7 cases were treated with glucocorticoid and human immunoglobulin, 6 cases were treated with tracheal intubation and ventilation, 2 case was treated with blood purification.

8. Discussion

Children have constituted a small fraction of recorded COVID-19 cases. However, relatively few cases of COVID-19 have been reported in children compared with the total number of cases in the general population. The first confirmed pediatric case of SARS-CoV-2 infection was reported in a familial cluster in Shenzhen on Jan 20, 2020[33]. This was a 10-year-old child with no symptom but presented radiological ground-glass lung opacities. With the progression of COVID-19 outbreak, the first infant case was reported from Xiaogan, Hubei province[21]. This was a 3-month-old female infant who had fever for one day and was admitted on January 26, 2020. As COVID-19 had reached epidemic proportions worldwide, the number of pediatric infections also increased concomitantly. Several studies have reported that the signs and symptoms of COVID-19 in children are similar to adults and are usually milder compared to adults[8,9,14,18,19]. However, no

comprehensive data are available on the impact of COVID-19 in children. It is reasonable to consider they might be at increased risk of severe disease even death[34].

In this review, we collected demographic, clinical, laboratory and imaging characteristics from 2,597 cases of COVID-19 in children, which included the largest sample number of pediatric patients by now. Of the cases, most children had exposure to household members with confirmed COVID-19. Illness among pediatric cases appear to be mild, as only 4.4% were severe and 0.9% were critical. Correspondingly, 14% were severe and 5% were critical in adults[35]. The primary symptoms in Children are similar as those in adults[36-39],but have lower incidence rates: fever occurred in 82-98.6% of adults but in 43.1% of children; cough occurred in 59.4-82% of adults but in 43.4% of children. Respiratory symptoms in children were mild, as 12.6% cases had tachypnea/shortness of breath, which occurred in 31% adult cases[38]. Other studies also reported that 55% of adult patients developed dyspnea[36], and 17% patients developed acute respiratory distress syndrome (ARDS), which were rarely observed in children. However, symptom of digestive tract appeared more common in children, as diarrhea occurred in 6.6% of pediatric patients from our analysis, but in 2-3.8% of adult cases from some clinical studies [36-38] The different patterns of clinical features in respiratory system and digestive tract might result from the maturity and functional discrepancy of SARS-CoV-2 receptor ACE2 between children and adults[40]. However, more studies are still required to prove this hypothesis.

There is lack of particular laboratory findings in COVID-19 until now. However, some indicators presented in different patterns between children and adults should be taken into our concern. Lymphopenia is the most common lab finding in adults with COVID-19, which was found in as many as 70.3-83% of hospitalized patients[36-39]. But in children, lymphopenia was only observed in 9.8% cases. Procalcitonin (PCT) increased in 40.8% pediatric patients in our review, but appeared normal in some other cases[28],It's worth pointing out that 0-0.05 ng/ml of PCT is the normal range for laboratory testing. However, between 0.05-0.5 ng/ml unlikely support the diagnosis of significant bacterial infection, as localized infections (without systemic signs) and allergic reaction may be associated with such low levels. For clinical diagnosis, it is tending to use the levels above 0.5 ng/ml, which are highly suggestive of systemic bacterial infection/sepsis or severe localized bacterial infection, such as severe pneumonia, meningitis, or peritonitis[41]. The discrepancy of reference ranges would result in different conclusions. PCT was typically normal in adults, but may increase among those admitted to the ICU[36,38,39]. Some children had leukocytosis (8.8%), elevated serum alanine aminotransferase (ALT, 11.2%) and aspartate aminotransferase (AST, 17.3%), elevated lactate dehydrogenase (LDH, 20.4%), high CRP (18.8%) and elevated D-dimer (12.1%), which were similar as those in adults that may be associated with greater illness severity[36,37,39,42-44]. A recent study analyzed the CK-MB level in venous blood of 273 patients with COVID-19[45]. The researchers found that elevated CK-MB occurred in 3.03% of mild cases, 5.00% of severe cases and 6.67% of critical cases, which indicated that higher concentration of CK-MB is associated with the severity and case-fatality rate of COVID-19. Notable is, elevated CK-MB occurred in 27.0% pediatric patients from our analysis, which implies that heart injury is more common to COVID-19 in children

than that in adults. However, renal injury was rare in children, as the indicators of renal function were normal in most of cases (~98%) from our analysis.

Bilateral air-space consolidation was demonstrated typically in patients with COVID-19, even though the chest radiographs are not remarkable in the early stage of disease[36,37,46]. Bilateral, peripheral ground glass opacities were also demonstrated typically in adults with COVID-19[38,42,46-55], which also occurred commonly in children. To date, there is still no specific CT imaging pattern for identifying COVID-19. Several studies identified chest CT abnormalities in patients were prior to the detections of SARS-CoV-2 RNA[46,56]. In children, there was a report that a 10-year-old boy with asymptomatic infection showed ground glass opacities on CT scan[33]. Another report of 31 children with SARS - CoV-2 infection show that 3 cases had no clinical manifestations, but with typical chest imaging manifestations. All of above suggested that chest imaging changes may be earlier than clinical symptoms, and also showed the value of chest imaging in early infection recognition and diagnosis of children with COVID-19[13].Given the much higher proportion of asymptomatic cases (7.6%) in children than that in adults (1%)[35], combining assessment of imaging features with clinical and laboratory findings could facilitate early diagnosis of COVID-19 pneumonia in children.

Children may play a role in the spread of SARS-CoV-2 in the community. As for children in China, SARS-CoV-2 nucleic acid (RNA) was detected in respiratory specimens up to 23 days[13] and in stools up to 43 days[28] after symptoms began. A case report of a 6-month-old infant with confirmed COVID-19 had no clinical signs or symptoms, except for a single transient temperature of 38.5°C. A high viral load of SARS-CoV-2 RNA was detected from the nasopharynx of this infant from the day of admission and remained positive up to 16 days[57]. Viral culture was not performed on specimens in the above reports. Therefore, it is uncertain whether persistent or asymptomatic RNA detection represented potentially transmissible virus.

This review may have some limitations according to the limited number of children cases with COVID-19, as well as the possible overlap of cases among the regarding articles. However, we revealed a comprehensive description including demographic, clinical, laboratory and imaging features of pediatric patients with COVID-19, especially the distinct pattern of manifestation for children when compared with adults, which provide a potent foundation for prevention, diagnosis, and treatment of COVID-19 epidemic in children.

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Conflict of interest

The authors have no Conflicts of interest to declare.

Authors' contributions

All authors contributed to the intellectual content of this manuscript and approved the final manuscript as submitted. Xiaojian Cui and Tongqiang Zhang drafted the initial manuscript. Jiafeng Zheng, Jiayi Zhang, Pi Si, Yongsheng Xu, Wei Guo, Zihui Liu, Wenliang Li, Jia Ma and Cuicui Dong searched literatures and collated data. Sijia He, Chunquan Cai and Yongming Shen revised the article critically for important intellectual content.

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Tables

Table 1. Demographic Characteristics and Illness Severity of COVID-19 in Children

Author	Journal [Ref #]	Case number (N)	Contact history (n/N)	Age Distribution (n/N)					Male (n/N)	Illness severity (n/N)					Death (n/N)
				<1 yr	1–5 yr	6–10 yr	11–15 yr	>15 yr		Asymptomatic	Mild	Moderate	Severe	Critical	
Lu et al.	NEJM [8]	171	156/171	31/171	40/171	58/171	42/171	0/171	104/171	27/171	33/171	107/171	0/171	3/171	1/171
Dong et al.	Pediatrics [9]	2143	2143/2143	379/2143	493/2143	523/2143	413/2143	335/2143	1213/2143	94/2143	1091/2143	831/2143	112/2143	13/2143	2/2143
Ma et al.	Chin J Contemp Pediatr [11]	115	105/115	14/115	36/115	32/115	33/115	0/115	73/115	61/115	5/115	46/115	0/115	3/115	0/115
Wang et al.	Chin J Pediatr [12]	34	28/34	N/A	N/A	N/A	N/A	N/A	14/34	3/34	9/34	22/34	0/34	0/34	0/34
Wang et al.	Chin J Pediatr [13]	31	31/31	N/A	N/A	N/A	N/A	N/A	N/A	4/31	13/31	14/31	0/31	0/31	0/31
Cai et al.	Clin. Infect. Dis. [14]	10	10/10	2/10	2/10	4/10	2/10	0/10	4/10	0/10	6/10	4/10	0/10	0/10	0/10
Feng et al.	Chin J Pediatr [15]	15	15/15	N/A	N/A	N/A	N/A	N/A	5/15	0/15	3/15	12/15	0/15	0/15	0/15

Su et al.	Emerg Microbes Infect. [16]	9	9/9	2/9	5/9	2/9	0/9	0/9	3/9	3/9	4/9	2/9	0/9	0/9	0/9
Zhou et al.	Chin J Contemp Pediatr [17]	9	9/9	3/9	6/9	0/9	0/9	0/9	4/9	5/9	0/9	4/9	0/9	0/9	0/9
Wei et al.	JAMA [18]	9	9/9	9/9	0/9	0/9	0/9	0/9	2/9	1/9	2/9	6/9	0/9	0/9	0/9
Zheng et al.	Curr Med Sci [32]	25	21/25	16/25†			9/25†		14/25	0/25	8/25	15/25	0/25	2/25	0/25
Summary of the case reports [19-31]		26	22/26	6/26	11/26	7/26	2/26	0/26	17/26	0/26	7/26	16/26	1/26	2/26	0/26
Total (%)		2597	2558/2597 (98.5)	446/2492 (17.9)	593/2492 (23.8)	626/2492 (25.1)	492/2492 (19.7)	335/2492 (13.4)	1453/2566 (56.6)	198/2597 (7.6)	1181/2597 (45.5)	1079/2597 (41.5)	113/2597 (4.4)	23/2597 (0.9)	3/2597 (0.1)

† Age distribution was grouped by using different criteria in this study: 1 month – 3 years, 3 – 6 years, ⩾6 years. We re-grouped these cases as <6 yr and ⩾6 yr in our review.

Table 2. Clinical Characteristics of COVID-19 in Children

Author	Journal [Ref #]	Case number (N)	Fever (n/N)	Cough (n/N)	Sore throat (n/N)	Tachycardia (n/N)	Rhinorrhea (n/N)	Nasal congestion (n/N)	Tachypnea (n/N)	Diarrhea (n/N)	Vomiting (n/N)	Myalgia or Fatigue (n/N)	Hypoxemia (n/N)	Chest pain (n/N)
Lu et al.	NEJM [8]	171	71/171	83/171	79/171	72/171	13/171	9/171	49/171	15/171	11/171	13/171	4/171	0/171
Ma et al.	Chin J Contemp Pediatr [11]	115	29/115	47/115	0/115	3/115	47/115	47/115	3/115	3/115	3/115	0/115	3/115	2/115
Wang et al.	Chin J Pediatr [12]	34	17/34	13/34	0/34	0/34	0/34	0/34	0/34	0/34	0/34	0/34	0/34	0/34
Wang et al.	Chin J Pediatr [13]	31	20/31	14/31	2/31	0/31	2/31	0/31	0/31	3/31	2/31	3/31	0/31	0/31
Cai et al.	Clin. Infect. Dis. [14]	10	8/10	6/10	4/10	0/10	2/10	3/10	0/10	0/10	0/10	0/10	0/10	0/10
Feng et al.	Chin J Pediatr [15]	15	5/15	1/15	0/15	0/15	0/15	1/15	0/15	0/15	0/15	0/15	0/15	0/15
Su et al.	Emerg Microbes Infect. [16]	9	2/9	1/9	0/9	0/9	0/9	0/9	0/9	0/9	0/9	0/9	0/9	0/9

Zhou et al.	Chin J Contemp Pediatr [17]	9	4/9	2/9	0/9	0/9	1/9	0/9	0/9	0/9	0/9	0/9	0/9	0/9
Wei et al.	JAMA [18]	7†	4/7	2/7	0/7	0/7	1/7	0/7	0/7	0/7	0/7	0/7	0/7	0/7
Zheng et al.	Curr Med Sci [32]	25	13/25	11/25	0/25	0/25	0/25	2/25	2/25	3/25	2/25	0/25	0/25	0/25
Summary of the case reports [19-31]		26	22/26	16/26	7/26	1/26	8/26	7/26	3/26	6/26	8/26	7/26	1/26	0/26
Total (%)		452	195/452 (43.1)	196/452 (43.4)	92/452 (20.4)	76/452 (16.8)	74/452 (16.4)	69/452 (15.3)	57/452 (12.6)	30/452 (6.6)	26/452 (5.8)	23/452 (5.1)	8/452 (1.8)	2/452 (0.4)

† 9 cases were reported in this study, but 2 of them had no clinical information available. So only 7 cases were collected into this table.

Table 3. Laboratory Characteristics of COVID-19 in Children

Author	Journal [Ref #]	Case number (N)	Normal WBC 5.5-12.0×10^9/L (n/N)	Leukocytosis >12.0×10^9/L (n/N)	Leukopenia <5.5×10^9/L (n/N)	Lymphopenia <1.2×10^9/L (n/N)	PCT >0.046 ng/ml (n/N)	CRP >10 mg/L (n/N)	LDH >300 U/L (n/N)	ALT >45 U/L (n/N)	AST >50 U/L (n/N)	Creatinine >62 μmol/L (n/N)	Blood urea nitrogen >7.1 mmol/L (n/N)	CK >170 U/L (n/N)	CK-MB >25 ug/L (n/N)	D-dimer >0.55 mg/L (n/N)
Lu et al.	NEJM [8]	171	N/A	N/A	45/171	6/171	105/171	33/171	N/A	21/171	25/171	N/A	N/A	N/A	N/A	21/171

Ma et al.	Chin J Contemp Pediatr [11]	115	88/115	4/115	23/115	15/115	N/A	N/A	N/A	11/115	N/A	N/A	N/A	N/A	34/115	N/A
Wang et al.	Chin J Pediatr [12]	34	28/34	5/34	1/34	1/34	1/34	1/34	10/34	N/A	N/A	N/A	N/A	N/A	N/A	3/34
Wang et al.	Chin J Pediatr [13]	31†	26/31	3/31	2/31	2/31	1/28	3/30	2/26	6/27	6/27	0/27	0/27	4/27	4/27	2/21
Cai et al.	Clin. Infect. Dis. [14]	10†	6/10	3/10	1/10	0/10	0/10	3/10	2/10	1/10	2/10	0/10	0/10	N/A	5/10	2/5
Feng et al.	Chin J Pediatr [15]	15	7/15	0/15	8/15	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Su et al.	Emerg Microbes Infect. [16]	9	8/9	1/9	0/9	0/9	0/9	0/9	N/A	0/9	0/9	0/9	0/9	N/A	6/9	0/9
Zhou et al.	Chin J Contemp Pediatr [17]	9†	7/9	2/9	0/9	0/9	N/A	3/7	3/5	0/9	4/9	0/9	0/9	N/A	N/A	0/9
Zheng et al.	Curr Med Sci [32]	25†	N/A	N/A	N/A	10/25	N/A	N/A	N/A	0/12	N/A	1/25	N/A	N/A	2/12	N/A
Summary of the case reports [19-31]		26†	16/26	4/26	8/26	8/26	4/20	11/26	3/23	3/23	6/23	1/11	1/11	1/20	2/23	5/23

Total (%)	445	186/249 (74.7)	22/249 (8.8)	88/420 (21.0)	42/430 (9.8)	111/272 (40.8)	54/287 (18.8)	20/98 (20.4)	42/376 (11.2)	43/249 (17.3)	2/91 (2.2)	1/66 (1.5)	5/47 (10.6)	53/196 (27.0)	33/272 (12.1)

† Case number of each item may differ, as every patient had distinct pattern of laboratory tests.

Table 4. Imaging Characteristics of COVID-19 in Children*

Author	Journal [Ref#]	Case number (N)	Normal	Ground-glass opacity	Local patchy shadow	Bilateral patchy shadow	Interstitial Lesions	White lung change	Pleural effusion
Lu et al.	NEJM [8]	171	60/171	56/171	32/171	21/171	2/171	0/171	0/171
Ma et al.	Chin J Contemp Pediatr [11]	115	66/115	47/115 (no specific classification available)				2/115	2/115
Wang et al.	Chin J Pediatr [13]	31	17/31	9/31	5/31	0/31	0/31	0/31	0/31
Cai et al.	Clin. Infect. Dis. [14]	10	6/10	0/10	4/10	0/10	0/10	0/10	0/10
Feng et al.	Chin J Pediatr [15]	15	6/15	9/15	0/15	0/15	0/15	0/15	0/15
Su et al.	Emerg Microbes Infect. [16]	9	7/9	1/9	1/9	1/9	0/9	0/9	0/9
Zhou et al.	Chin J Contemp Pediatr [17]	9	2/9	6/9	4/9	4/9	0/9	0/9	1/9

Zheng et al.	Curr Med Sci [32]	24†	8/24	1/24	5/24	11/24	0/24	0/24	0/24
Summary of the case reports [19-31]		25‡	6/25	5/25	9/25	6/25	0/25	0/25	0/25
Total (%)		409	178/409 (43.5)	87/294 (29.6)	60/294 (20.4)	43/294 (14.6)	2/294 (0.7)	2/409 (0.5)	3/409(0.7)

* Some patients may have 2 or more abnormalities of chest radiographs.

† There were 25 cases included in this study, only 24 of them were subjected to chest CT scans.

‡ There were 6 cases included in Ref#19, only 5 of them had imaging information. Totally 25 cases were collected in this group.

Table 5. Nucleic Acid Testing of SARS-CoV-2 RNA in Children with COVID-19

Author	Journal [Ref#]	Case number (N)	Time from illness onset to SARS-CoV-2 nucleic acid turned positive in different types of specimens (days)			Duration of SARS-CoV-2 shedding in different types of specimens (days)		
			Nasal and pharyngeal swab	Sputum	Fecal	Respiratory swabs	Anal swab	Stool
Dong et al.	Pediatrics [9]	2143	2 (0-42)	N/A	N/A	N/A	N/A	N/A
Wang et al.	Chin J Pediatr [13]	31	N/A	N/A	N/A	11 (7-23)	N/A	N/A
Cai et al.	Clin. Infect. Dis. [14]	10	N/A	N/A	6 (3-13)	12 (6-22)	N/A	20 (18-30)
Su et al.	Emerg Microbes Infect. [16]	9	N/A	N/A	N/A	11.2 (8-16)	N/A	N/A
Wei et al.	JAMA [18]	9	1-3	N/A	N/A	N/A	N/A	N/A

Liu et al.	NEJM [19]	6	4.7 (3-5)	N/A	N/A	7.5 (5-13)	N/A	N/A
Cai et al.	Chin J Pediatr [20]	1	1	N/A	N/A	12	N/A	N/A
Zhang et al.	Chin J Pediatr [21]	1	1	N/A	N/A	10	N/A	>14
Ji et al.	World Journal of Pediatrics [22]	2	1.5	N/A	N/A	N/A	N/A	N/A
Zhang et al.	Chin J Contemp Pediatr [23]	2	2	N/A	N/A	10	N/A	N/A
Wang et al.	Chin J Contemp Pediatr [24]	1	7	N/A	N/A	3	5	N/A
Zhao et al.	Zhejiang Medical Journal [25]	1	N/A	5	N/A	17	>20	>20
Zeng et al.	Chin J Pediatr [26]	1	8	N/A	N/A	N/A	N/A	N/A
Zhang et al.	World Latest Medicine Information [27]	1	1	N/A	N/A	7	N/A	N/A
Zhang et al.	J Med Virol. [28]	3	7 (1-14)	N/A	N/A	11 (11-14)	N/A	37 (34-43)
Zeng et al.	JAMA Pediatrics [29]	3	2	N/A	N/A	4	5	N/A
Xing et al.	Pre-print [30]	3	N/A	N/A	N/A	13	N/A	30 (23-33)
Chen et al.	Chin J Pediatr [31]	1	14	N/A	N/A	N/A	N/A	N/A