Review Article

Respiratory Manifestations of COVID-19 in Children: A Narrative Review

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ABSTRACT

Background: Coronavirus disease 2019 (COVID-19, the seventh coronavirus) is a new infectious disease that spread worldwide and rapidly became a pandemic. COVID-19 is rare in children and often asymptomatic. The respiratory system is mainly involved in COVID-19 infection.

Objectives: This study aimed to review respiratory manifestations in children with COVID-19.

Methods: We searched for studies published from January 2020 to January 2021 in PubMed, Google Scholar, and Scopus in English. The search words were "2019-nCoV," "novel coronavirus," "COVID-19," "SARS-CoV-2," "severe acute respiratory syndrome coronavirus 2," "children," "child," "infant," "teenager," "adolescent," "pediatric," and "neonate."

Results: Cough was a common symptom in our study (18.8%-100%, mean=64%). Pneumonia prevalence in children with COVID-19 is 11%-67% (mean=46%). Mild respiratory symptoms (14% - 60%) and severe respiratory distress syndromes (14%) were reported in some studies. Upper respiratory tract infection (URTI) was reported in 4 studies ranging from 11.1% to 34.4% (mean=24.1%). Ground-glass opacities (GGO) was reported in 12.2% to 81% of cases (mean=49.01%). Isolated consolidations were reported in 17% and 58% of patients in two studies. Enhanced lung texture was reported in 1.3% to 50% (mean=20.07%) of patients. Bilateral patchy shadowing was seen in 12.3% to 68% (mean=46.58%) of patients.

Conclusions: Cough is the most common manifestation of respiratory system involvement in children with COVID-19. GGO and bilateral patchy involvement are the most common finding on lung CT scans in children with COVID-19.

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1. Introduction

Coronavirus disease 2019 (COVID-19, the seventh coronavirus) is a new infectious disease that spread rapidly worldwide and became a pandemic (incubation period: usually 1 to 14 days, up to 24 days). The disease is caused by the "severe acute respiratory syndrome coronavirus 2" (SARS-Co2). Structural proteins of COVID19 are spike (S), membrane (M), envelope (E), and nucleocapsid (N). The virus binds to a human cell receptor that expresses angiotensin-converting enzyme 2 (ACE2), then it internalizes, replicates, and new virions are released from the infected cell (1). Mild to severe cases of pneumonia due to novel enveloped RNA coronavirus (COVID-19, SARS-CoV-2) were found firstly in Wuhan, China. COVID-19 is rare in children and often asymptomatic. Children tested positive for COVID-19 in 1.2% - 5% of diagnosed cases in Italy, China, and the United States (2-4). Neonates and children of all ages can be affected with no sex predominance.

The virus is transmitted mainly through respiratory droplets and close contact. Also, it is transmitted through the conjunctiva, digestive tract, and probably vertically from the mother to the child (5). Most children infected with COVID-19 have contracted the virus in a family contact setting (5). COVID-19 has a milder course in children than in adults due to less mature angiotensin-converting enzyme (ACE) 2, lower inflammatory markers, and a low rate of lymphocytopenia. Death is rare in children with COVID-19, and it happens in children with underlying conditions (6-8). The respiratory system involvement in COVID-19 infection ranges from asymptomatic and or mild pneumonia (81%) to less common severe (14%) or critical (5%) form (9). People with underlying disorders such as uncontrolled asthma (moderate to severe stages) have a risk factor for COVID-19 infection (10). Also, respiratory symptoms (rhinorrhea, congestion, sore throat, cough, or shortness of breath) are more common (76%) in children with COVID-19 infection (11). Cough was the predominant presentation (54%) in children with COVID-19 (11). Due to the numerous and various clinical and radiographic respiratory reports, this narrative study aims to review respiratory manifestations and lung CT scan findings in children with COVID-19.

2. Materials and Methods

We searched studies published from January 2020 to January 2021 on PubMed, Google Scholar, and Scopus in the English language, using the keywords of "2019-nCoV," "novel coronavirus," "COVID-19," "SARS-CoV-2," "children," "child," "infant," "teenager," "adolescent," "pediatric," and "neonate." Children were defined as individuals under 20 years of age. All available studies involving observational studies, cohort studies, case series, and reviews that reported clinical and imaging information were included. The recruited subjects must have SARS-CoV-2 infection confirmed through real-time reverse transcriptase-polymerase chain reaction (RT-PCR), imaging, or clinical manifestations. We included full text and English language articles in this study. We used 30 articles for writing our review.

3. Results

After the study search, we found 19 articles that met our criteria for conducting this review (Tables 1 and 2). Cough was the most common symptom reported in the studies we reviewed (18.8%-100%, mean=64%) (4, 12-29). Pneumonia in children with COVID-19 was reported between 11% and 67% (mean=46%) in these studies (2, 4, 14, 19, 20, 22, 24, 25, 27). Mild respiratory symptoms were variable and presented in 14% to 60% of patients (4, 27) and severe respiratory distress syndrome in 14% as reported in some studies (4). Upper respiratory tract infection (URTI) was reported in 4 studies ranging from 11.1% to 34.4% of patients (mean=24.1%) (14, 15, 24, 27).

Rhinorrhea was relatively common in children, occurring in 9% to 20% of patients (mean=13.07%) (13, 14, 17, 20, 25, 28, 29). Nasal congestion were also reported in these studies, accounting for 1.1% to 30 % of patient presentations (mean=12.12%) (13-15, 18, 27-29). Tachypnea was reported in 0% to 40% of patients (mean=29.4%) (14, 17-21, 23-29). Sore throat was reported in 0% to 40% (mean=9.93%) of patients (13, 15, 17, 18, 23, 24, 26, 29). Anosmia was reported in only one study, in 30% of patients (13). Sneezing was reported in two studies in 0.7% and 7.4% of their patients (18, 29).

Radiographic finding

Ground-glass opacities (GGO) was reported in 12.2% to 81% of cases (mean=49.01%) (4, 14, 16, 17, 19, 20, 23-25). Isolated consolidation was reported in 17% and 58% of patients in two studies (20, 25). Enhanced lung texture was seen in 1.3% to 50% of patients (mean=20.07%) (4, 14, 16, 17, 19, 20, 21, 25). Bilateral patchy shadowing was seen in 12.3% to 68% of cases (mean=46.58%) (14, 16, 17, 19-21, 24-27). Unilateral patchy shadowing was reported in 18.7% to 55% of patients (mean=34.4%) (14, 16, 17, 19, 20, 21, 26, 27).

Table 1. Upper and Lower respiratory manifestations of COVID-19 in children

Author Symptom	Liu12	Jiatong4	Jiehao13	Lu14	Ranabothu15	Li16	Xia17	GUO18	Song19	Caro-Dominguez20
Cough, %	100		60	48.5	15.4	59	65	32.4	18.8	55
Pneumonia, %	67	21		65					44	67
MRS		14								
SRS		14								
URTI				19	11.1					
Rhinorrhea			20	7.6			15			14
Nasal congestion			30	5.3	1.1			2.2		
Tachypnea on admission				28.7			10	2.2	0	36
Sore throat			40		4.3		5	2.2		
Loss of smell					2.1					
Sneezing								0.7		

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MRS: mild respiratory symptom; SRS: severe respiratory distress syndrome; URTI: upper respiratory tract infection.

Pleural effusion was reported in 3% to 10% of patients (mean=6.66%) (20, 21, 25).

Atelectasis and pneumothorax were reported in 2% of children (20). RLL and LLL involvements were seen in 41% and 27% of patients respectively in Li study (16). RLL and LLL involvements were both reported in 71% of patients respectively in Caro-Dominguez\s study (20). RUL involvement was reported in 6% to 21% in children with COVID-19 (16, 24, 25).

Table 1. Upper and Lower Respiratory Manifestations of COVID-19 in Children (Continued)

Author Symptom	Kainth21	Su22	Qiu23	Wu24	Mahmoudi25	Du26	ZHENG27	Alsayed28	Yu 29
Cough, %	49		19	32.4	80	21.4	44	48.5	31.3
Pneumonia, %		11		40.6	40		60		
MRS							60		
SRS									
URTI				34.4			32		
Rhinorrhea					9			10	8.9
Nasal congestion							8	10	7.4
Tachypnea on admission	35		3	2.7	40	0	8	28.7	16.4
Sore throat			6	0		7.1			14.9
Loss of smell									
Sneezing									7.4
Rhonchi and crackles				21.6					

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MRS: mild respiratory symptom; SRS: severe respiratory distress syndrome; URTI: upper respiratory tract infection.

Table 2. Types of pulmonary involvement and distribution of different parts of lung in children with COVID-19

Author Finding	Jiatong4	Lu14	Li16	Xia17	Song 19	Caro-Dominguez20	Kainth21
GGO, %	70.4	32.7	14	60	43.8	81	
Consolidation						58	
Enhanced lung texture, %	7.4	1.3	9	50	37.5	16	32
Bilateral patchy shadowing		12.3	68	50	18.8	63	67
Unilateral patchy shadowing		18.7	23	30	50	55	33
Pleural effusion						7	10
Pneumothorax						2	
Atelectasis						2	
RUL			9				
RLL			41			71	
LUL			14				
LLL			27			71	

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GGO: ground-glass opacities; RUL: right upper lobe; RLL: right lower lobe; LUL: left upper lobe; LLL: left lower lobe.

4. Discussion

SARS-CoV-2 affects many organs, including the respiratory system in children. Respiratory symptoms were reported in 51% of children with COVID-19 (30). In this study, we analyzed respiratory clinical and chest radiographic manifestations of COVID-19 in children. Overall, pediatric patients with COVID-19 have a good prognosis and recover within one to two weeks. Children of all ages, including neonates, are affected by COVID-19. Most children contract COVID-19 from adult family members in their households (31). Also, acute upper respiratory infection is common in children (15). Our study showed that cough is the most common manifestation of the respiratory system in children with COVID-19 (mean=64%) (4, 12-29). Another review study reported the prevalence of cough to be around 40% in children with COVID-19 (32). Daun Yn et al. reported that cough is the most common clinical manifestation in children with COVID-19 (33). Cough was also the most common symptom in patients with COVID-19 as in Patel et al.'s study (11.1% and 100% of cases) (mean=48%) (34), Nipunie's study (50%-80%) (35), and Yudan ding's study (7%-75 %) (36). Fever (59·1%) and cough (55·9%) are the most common symptoms in children with COVID-19 (37, 38). Viral pneumonia (11%-67%, mean=46%) is a common finding in children with COVID-19 in our study (4, 12, 14, 19, 20, 22, 24, 25, 27). Pneumonia was observed in the majority (65%) of children (39). Fortunately, mild respiratory symptoms (14%-60%) (4, 27) were more common than severe respiratory distress syndromes (14%) (4). In another review, mild and moderate respiratory infections were seen in 37% and 45% of the patients, respectively, but the severe infection was rare (3%) (32). In Wang's study, 50.9%, 38.8%, 5.2%, and 0.6% of patients developed mild, moderate, severe, and critical illnesses, respectively (40).

URTI is a relatively common manifestation found in 11.1% to 34.4% of the patients (mean=24.1%) (14, 15, 24, 27). Therefore, URTI may be observed before or concurrent with lower respiratory symptoms. Rhinorrhea was not a standalone symptom in patients observed in these studies but is a relatively common symptom alongside other disease manifestations in children with COVID-19. Rhinorrhea was observed in 9% to 20% of patients (mean=13.07%) (13, 14, 17, 20, 25, 28, 29). This result is similar to Assaker's report of COVID-19 symptoms in children (16%) (32). In our review, the nasal congestion was commonly observed (12.12%) (14, 15, 18, 27, 28), but Rajapakse et al. study reported it in around 4%-30% of cases (35), Ding et al. in 0% to 54% (36), and Hoang et al. in 20% of cases (38). Therefore, the combination of nasal congestion/rhinorrhea is a relatively common symptom in children with COVID-19. Accounts of tachypnea was very variable ranging from 0% to 40%

Table 2. Types of pulmonary involvement and distribution of different parts of lung in children with cOVID0-19 (continued)

Author Findings	Qiu23	Wu24	Mahmoudi25	Du 26	ZHENG27
GGO, %	53	12.2	74		
Consolidation			17		
Enhanced lung texture, %			7.4		
Bilateral patchy shadowing		43.2	31	54.5	48
unilateral patchy shadowing				45.5	20
Pleural effusion			3		
Pneumothorax					
Atelectasis					
RUL		21	6		
RLL		21	9		
LUL		35			
LLL		35	3		

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GGO: ground-glass opacities; RUL: right upper lobe; RLL: right lower lobe; LUL: left upper lobe; LLL: left lower lobe.

(mean=29.4%) (14, 17-21, 23-29). Other studies reported tachypnea in 0% to 50% of patients (34); shortness of breath was reported in 13% to 30% of patients (35). Ding et al. reported Dyspnea and tachypnea in 3%-28% of their cases (36). Dyspnea and/or shortness of breath were seen in 11.7% of Hoang et al.'s patients (38). Therefore, we observed tachypnea with more severe respiratory involvement when admitted to the hospital. Sore throat also is another symptom in patients with COVID-19 (0%-40%) (mean=9.93%) (13, 15, 17, 18, 23, 24, 26, 29). Other review studies reported sore throat of around 14% in Assaker's study (32), sore throat/pharyngeal erythema combination of around 28.6% in Patel's study (34), 5%-50% in Rajapakse's study (35), 3% to 46% in Ding's study (36), and sore throat of 18.2% in Hoang's study (38).

Son et al. reported respiratory symptoms and sore throat in 21%-65% AND 10% of covid19 patients, respectively (41). The pharyngeal erythema and sore throat, either alone or together, are relatively common. However, sneezing can be one of the manifestations of COVID-19 infection in children. Two studies reported sneezing in 0.7% and 7.4% of their patients, respectively (18, 29). Also, sneezing (23%) was common in Assaker's review study (32). In a review study, rhinorrhea, sneezing, and nasal congestion rate was 6.5% to 40% (34). Less common respiratory symptoms are nasal congestion, runny nose, and sore throat (13, 15, 29, 32, 33). Often these manifestations (sneezing, rhinorrhea, nasal congestion) were concurrent with other manifestations. Loss of smell was reported only in one study in our review (2.1%) (15); therefore, we cannot comment on the significance of this symptom in COVID-19. Dyspnea, cyanosis, acute respiratory distress syndrome (ARDS), respiratory failure, and multiple organ dysfunction syndromes (MODS) are rare other findings in children with COVID-19 (33). Severe pneumonia criteria include hypoxia (SpO2≤93% or <90% in premature infants), increased respiration rate (RR≥70/min in ≤1 year old, RR≥50/min in >1 year old), and blood gas analysis of PaO2<60 mm Hg and PaCO2>50 mm Hg (25).

Chest radiography is not conclusive for diagnosing COVID-19 in children because it is normal in mild lung involvement (20). The chest x-ray is the first-line imaging for lung involvement, with the most common finding being increased central peribronchovascular markings and airspace consolidation (20). Chest x-ray abnormality was seen in 57.1% of the cases (34). Chest radiography was normal in 31%, consolidation was seen in 11%, ground-glass opacities in 40%, and central distribution in 20%. Diffuse distribution was more common (31%) with involvement in LLL (6%), RLL (6%), RML (3%), RML/LLL (6%), RUL/LLL (3%), RUL/RML (6%), and RUL/RML/RLL/LLL (3%) (25). In Guo's study, abnormal chest radiography was seen in 30% of patients (18). Bronchial

thickening, ground-glass opacities, and inflammatory lung lesions were seen in chest radiographic pictures (plain and CT scan) (37, 42). However, the chest x-ray usually is non-specific and may be normal in the early phases of the disease (1).

Chest computed tomography (CT) scan might have good potential screening and diagnosis of COVID-19. The CT scan manifestations of COVID-19 in children have diverse specificity (33). GGO is the most common finding in lung CT scan in children with COVID-19 in our study from 12.2% to 81% (mean=49 01%) (33-36, 38, 39, 42). Typical chest CT findings in children included unilateral or bilateral, peripherally located GGOs (33, 35). Ground-glass opacities and consolidation is the typical radiographic image of pulmonary involvement in COVID-19 (43). Computed tomography (CT) of the chest is more sensitive and shows peripheral multiple small plaques and interstitial changes, bilateral multiple GGO and or infiltrating shadows, lung consolidation with a surrounding halo, which is a typical finding in the pediatric patient (1).

Bilateral patchy shadowing is the most common finding on lung CT scan in children with COVID-19 from 12.3% to 68% (mean=46.58%) in our study (14, 16, 17, 19-21, 24-27) than unilateral patchy shadowing which was 18.7% to 55% (mean=34.4%) (14, 16, 17, 19-21, 26, 27). Focal (14%), multifocal (68%), and diffuse (9%) patterns were seen on the lung CT scan in Li`s study (16). GGO, mainly in the peripheral and posterior lungs, is a more common finding in children (33, 34). Less common findings are GGO + interlobular septal thickening and consolidation alone. It is recommended that a low-dose CT scan should be performed on an infant and not be repeated (33). Unilateral CT imaging findings were present in 36% of cases, while 64% of pediatric patients with COVID-19 had bilateral findings (34).

In Li\s study there was 41% and 27% involvement in RLL and LLL respectively (16). Caro-Dominguez et al. reported 71% involvement for both LLL and RLL (20). RUL involvement in children with COVID-19 has been reported anywhere between 6% to 21%. (16, 24, 25). In another study, LLL/RUL was involved in 14%, RLL/LLL in 11%, RLL/RML in 9%, and RLL/RUL/LLL/LUL in 3% of cases (35). Asymptomatic children have been reported to have abnormal CT findings (39). Chest imaging could be abnormal while the child is subclinical (4). Chest CT images of 69% of cases suggest COVID-19 with a negative RT-PCR test (35). Pleural effusion was reported as a rare finding in children (1, 33). But in our study, pleural effusion was reported in 3% to 10% of cases (mean=6.66%) (20, 21, 25). In one study, we found atelectasis and pneumothorax in children with COVID-19 in 2% (20). There is little evidence that lung ultrasound useful diagnosis of pneumonia in children (20). The study limitation is that it is a narrative review, and the authors selected some articles. We suggested a systematic and meta-analysis study.

5. Conclusion

Cough is the most common manifestation of the respiratory system involvement in children with COVID-19. Pneumonia and tachypnea also are common manifestations. Rhinorrhea, nasal congestion, sore throat, and sneezing are less common clinical manifestations. Therefore, all parts of the upper and lower respiratory system can be involved. GGO and bilateral patchy involvement are the most common findings on lung CT scans in children with COVID-19. Pleural effusion is a rare finding in patients.

Ethical Considerations

Compliance with ethical guidelines

All ethical principles are considered in this article.

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Authors' contributions

Conceptualization, original idea, study concept, design, and manuscript writing: J.Gh; Data gathering, study design, and manuscript writing: F.M and A.D; Revision of manuscript: N.Gh.

Conflicts of interest

The authors declared no conflict of interest.

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