Systematic Review and Meta-Analysis

Medicine®

OPEN

Computed tomography features of COVID-19 in children

A systematic review and meta-analysis

Ji-gan Wang, MD[a,*], Yu-fang Mo, MD[b], Yu-heng Su, MD[a], Li-chuan Wang, MD[a], Guang-bing Liu, MD[a], Meng Li, MD[a], Qian-qiu Qin, MD[a]

Abstract

Background: There are few reports on the chest computed tomography (CT) imaging features of children with coronavirus disease 2019 (COVID-19), and most reports involve small sample sizes.

Objectives: To systematically analyze the chest CT imaging features of children with COVID-19 and provide references for clinical practice.

Data sources: We searched PubMed, Web of Science, and Embase; data published by Johns Hopkins University; and Chinese databases CNKI, Wanfang, and Chongqing Weipu.

Methods: Reports on chest CT imaging features of children with COVID-19 from January 1, 2020 to August 10, 2020, were analyzed retrospectively and a meta-analysis carried out using Stata12.0 software.

Results: Thirty-seven articles (1747 children) were included in this study. The heterogeneity of meta-analysis results ranged from 0% to 90.5%. The overall rate of abnormal lung CT findings was 63.2% (95% confidence interval [CI]: 55.8%–70.6%), with a rate of 61.0% (95% CI: 50.8%–71.2%) in China and 67.8% (95% CI: 57.1%–78.4%) in the rest of the world in the subgroup analysis. The incidence of ground-glass opacities was 39.5% (95% CI: 30.7%–48.3%), multiple lung lobe lesions was 65.1% (95% CI: 55.1%–67.9%), and bilateral lung lesions was 61.5% (95% CI: 58.8%–72.2%). Other imaging features included nodules (25.7%), patchy shadows (36.8%), halo sign (24.8%), consolidation (24.1%), air bronchogram signs (11.2%), cord-like shadows (9.7%), crazy-paving pattern (6.1%), and pleural effusion (9.1%). Two articles reported 3 cases of white lung, another reported 2 cases of pneumothorax, and another 1 case of bullae.

Conclusions: The lung CT results of children with COVID-19 are usually normal or slightly atypical. The lung lesions of COVID-19 pediatric patients mostly involve both lungs or multiple lobes, and the common manifestations are patchy shadows, ground-glass opacities, consolidation, partial air bronchogram signs, nodules, and halo signs; white lung, pleural effusion, and paving stone signs are rare. Therefore, chest CT has limited value as a screening tool for children with COVID-19 and can only be used as an auxiliary assessment tool.

Abbreviations: ACE2 = angiotensin-converting enzyme 2, CI = confidence interval, COVID-19 = coronavirus disease 2019, CT = computed tomography, SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Keywords: children, computed tomography features, COVID-19, SARS-CoV-2

1. Introduction

In January 2020, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was identified as the cause of a series of pneumonia cases first diagnosed in Wuhan, Hubei Province, China.[1] Soon after, SARS-CoV-2 spread all over the world.[2] By March 2020, the spread of coronavirus disease 2019 (COVID-19) was recognized as a pandemic by the World Health Organization.[3] In the early stages of the pandemic, it was thought that children were not easily infected[1]; however, as the pandemic has progressed, the number of pediatric cases has gradually increased. Many infected children are asymptomatic, but some patients have fever, dry cough, and fatigue, while others have gastrointestinal symptoms, including abdominal discomfort, nausea, vomiting, abdominal pain, and diarrhea.[4] Computed tomography (CT) is a sensitive tool for diagnosing symptomatic COVID-19 patients. In adult patients, the most common CT manifestation is ground-glass opacities. Other CT manifestations, such as air bronchography, lymph node enlargement, and effusion, are less common.[5] Among the 1014 hospitalized patients with obvious symptoms from Wuhan, China, the CT scans of most patients were abnormal; however, with a sensitivity of 97% and specificity of 25%, the

Editor: Vasile Valeriu Lupu.

This work was supported by Self-Funded Scientific Research Project of Guangxi Zhuang Autonomous Region Health Commission (Nos. Z20210123).

The authors declare no conflict of interest.

Supplemental Digital Content is available for this article.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

[a] Maternal and Child Health Hospital of Guangxi Zhuang Autonomous Region, Nanning, China, [b] Liuzhou Workers' Hospital, Liuzhou, China.

[*] Correspondence: Ji-gan Wang, 59 Xiangzhu Avenue, Xingning District, Nanning 530003, Guangxi Zhuang Autonomous Region, China (e-mail: wangjigan@163.com).

How to cite this article: Wang Jg, Mo Yf, Su Yh, Wang Lc, Liu Gb, Li M, Qin Qq. Computed tomography features of COVID-19 in children: a systematic review and meta-analysis. Medicine 2021;100:38(e22571).

Received: 10 September 2020 / Received in final form: 30 May 2021 / Accepted: 6 September 2021

http://dx.doi.org/10.1097/MD.0000000000022571

false positive rate was very high.[6] Compared with adults, children have relatively mild symptoms, so CT is not very typical.[7] However, there are few reports on pediatric CT features, and most reports involve small sample sizes. In addition, larger pediatric cohort studies have not been comprehensive enough.[8] Therefore, the lung CT features of children with COVID-19 has been reviewed systematically in this study.

2. Evidence acquisition

2.1. Registration

This systematic review and meta-analysis was registered in the Prospero International Prospective Register of Systemic Reviews (CRD42020196602).

2.2. Literature search strategy

A literature search was conducted through PubMed, Web of Science, Embase, Johns Hopkins University published data, as well as the Chinese databases CNKI, Wanfang, and Chongqing Weipu between January 1, 2020 and August 10, 2020 to collect reports on the characteristics of chest CT of children with COVID-19. Concurrently, online database and manual retrieval were used, and the references included in the literature were traced. Subject-specific and free words were used in the retrieval, and adjustments were made according to the characteristics of the different databases without limitations to language, race, or region. The following search terms were used: "children," "child," "kid," "pediatric" in association with "clinical feature" OR "epidemiology" OR "Imaging" OR "CT" and "2019-nCoV" OR "COVID-19" OR "SARS-CoV-2" OR "Corona Virus Disease 2019."

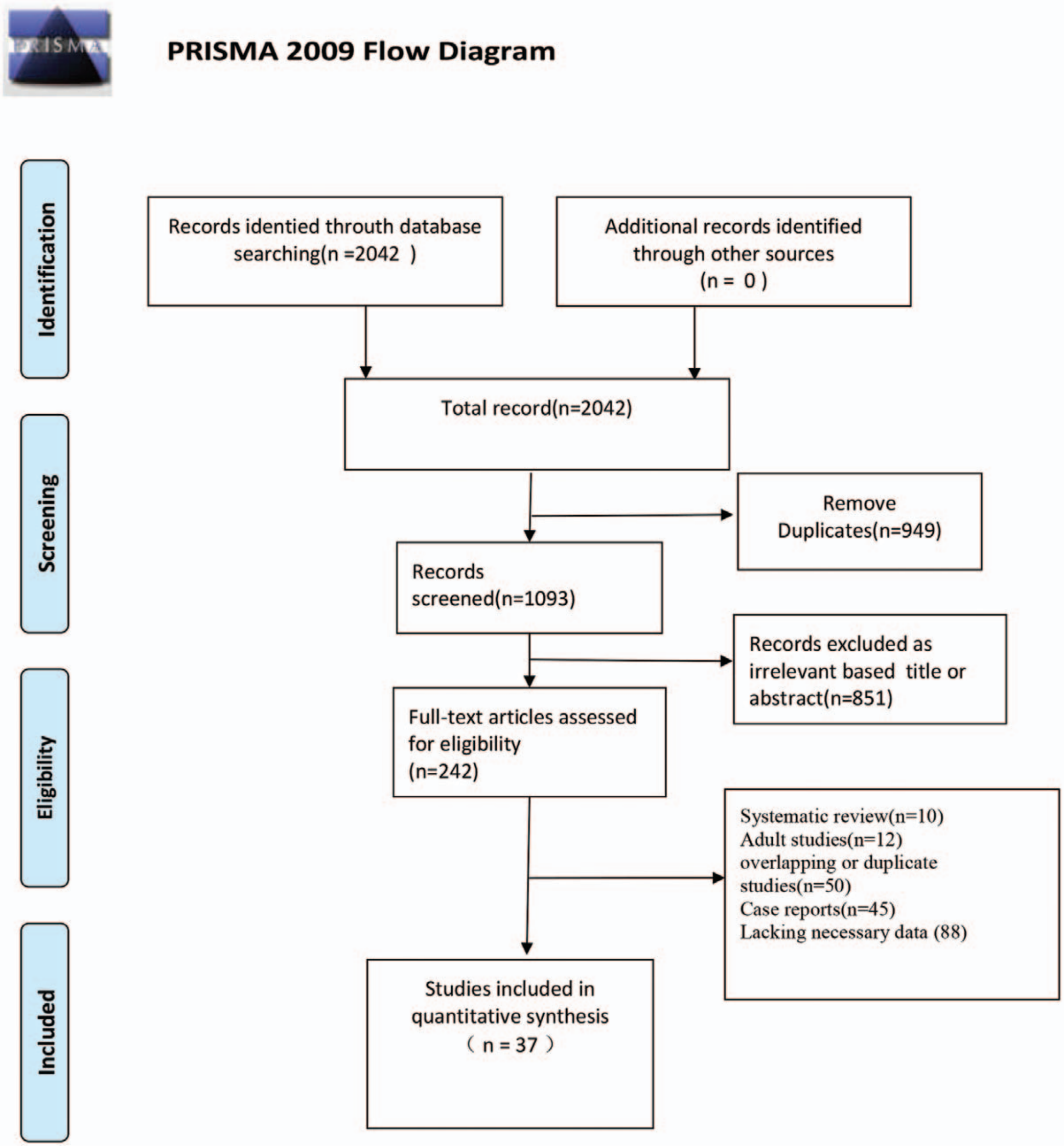

Figure 1. The flowchart of study selection.

Table 1

Basic fratures of the included studies.

Author	Region or country	Period of inclusion of patients	Research type	Total number of people	Male (n)	Female (n)	Age group	Number of computed tomography examinees	Outcome indicator
Ma et al[10]	Wuhan Children's Hospital, China	By February 27, 2020	Retrospective	115	73	42	Range: 51 days–15 years	115	①②③④
Wang et al[11]	Shiyan City, China	January 20–February 15, 2020	Retrospective	20	6	14	Median age: 12.9 years Range: 2 months–310 years	20	①③④
Wu et al[12]	Jiangxi Province, China	January 27–March 4, 2020	Retrospective	23	9	14	Median age: 5.7 years Range: 3 months–17.8 years	22	①③④
Cao et al[13]	Shandong Province, China	January 26–February 29, 2020	Retrospective	37	20	17	Range: 0–18 years	21	①③④
Zhou et al[14]	Shenzhen, China	January 20–February 10, 2020	Retrospective	9	4	5	Median age: 1 year Range: 7 months–3 years	9	①③④
Xiong et al[15]	Chongqing Qingsanxia Central Hospital, China	February 2–15, 2020	Retrospective	4	2	2	Average age: 2 years and 10 months	4	①③
Ma et al[16]	Wuhan Maternal and Child Health Hospital, China	January 25–February 5, 2020	Retrospective	22	12	10	Median age: 4 years Range: 2 months–4 years	22	①③④
Zhong et al[17]	Changsha, China	January 20–February 15, 2020	Prospective observational study	9	4	5	Range: 3 months–15 years	9	①③
Li et al[18]	Yichang, China	January 16–March 14, 2020	Retrospective	22	12	10	Average age: 6 years	22	①③④
Li et al[19]	Zhongshan No.5 Hospital, China	January 28–February 8, 2020	Prospective observational study	5	3	2	Average age: 3.4 years Range: 10 months–6 years of age	5	①
Song et al[20]	Hubei Xiangyang Central Hospital, China	January 1–March 17, 2020	Retrospective	16	10	6	Median age: 8.5 years Range: 11 months–14 years	16	①③④
Zhu et al[21]	Jiangsu Province, China	January 24–February 22, 2020	Retrospective	10	5	5	Average age: 9 years and 2 months	10	①
Liu et al[22]	The First Affiliated Hospital of Chongqing, China	January 20–February 9, 2020	Retrospective	5	4	1	Average age: 6 years	5	①③④
Li et al[23]	Xiangyang First People's Hospital and Taihe Hospital, China	January 26–February 20, 2020	Retrospective	8	3	5	Median age: 2.5 years Range: 1–5 years	8	①③④
Steinberger et al[24]	6 hospitals in China	January 23–February 8, 2020	Retrospective	30	15	15	Median age: 10 years Range: 10 months–18 years	30	①③④
Lu et al[25]	Guangzhou Maternal and Child Health Hospital, China	January 22–February 9, 2020	Retrospective	9	5	4	Average age: 7.8±5.3 years Range: 2 months–15 years	9	①③④
Lan et al[26]	Wuhan Zhongnan Hospital	January 20–February 28, 2020	Prospective observational study	4	2	2	The average age is 10 years	4	①④
Soltani et al[27]	Hamadan and Sanandaj, west of Iran	March 1–April 15, 2020	Retrospective	30	14	16	Median age: 6±5 years Range: 1 day–15 years	30	①③④
Feng et al[28]	The Third People's Hospital of Shenzhen, China	January 16–February 6, 2020	Retrospective	15	5	10	Average age: 7 years Range: 4–14 years	15	①④
Wang et al[29]	Six provinces in northern China	January 25–February 21, 2020	Retrospective	31	N	N	Average age: 7 years and 6 months Range: 6 months–17 years	31	①③④
Rahimzadeh et al[30]	North of Iran		Retrospective	9	6	3	Range: 2–10 years	9	①③④
Bai et al[31]		January 29–March 12, 2020	Retrospective	25	14	11	Median age: 11 years Range: 0.6–17.0 years	25	①④

(*continued*)

Table 1
(continued).

Author	Region or country	Period of inclusion of patients	Research type	Total number of people	Male (n)	Female (n)	Age group	Number of computed tomography examinees	Outcome indicator
	Four designated treatment hospitals in Chongqing, China								
Zheng et al[32]	Ten hospitals in Hubei, China	February 1–10, 2020	Retrospective	25	14	11	Median age: 3 years Range: 3 months–14 years	25	①
Toubiana et al[33]	Necker Hospital for Sick Children in Paris, France	April 27–May 1, 2020	Prospective observational study	21	9	12	Median age: 7.9 years Range: 3.7–16.6 years	18	①
Korkmaz et al[34]	Bursa City Hospital, northwest Turkey	March 5–May 5, 2020	Retrospective	81	N	N	Median age: 9.50 years Range: 0–17.75 years	81	①
Qiu et al[35]	Three hospitals in Zhejiang, China	January 17–March 1, 2020	Retrospective	36	23	13	Average age: 8.3 ± 3.5 years	36	①
Götzinger et al[36]	21 European countries	April 1–24, 2020	Retrospective	582	311	271	Median age: 5 years Interquartile range: 0.5–12.0 years	198	N
Zachariah et al[37]	New York-Presbyterian Morgan Stanley Children's Hospital	March 1–April 15, 2020	Retrospective	50	27	23	Median age: 9 years Range: 6 days–21 years	36	①③④
Gaborieau et al[38]	Suburbs of Paris	March 23–May 10, 2020	Prospective observational study	157	94	63	Median age: 1 year Range: 0.125–11 years	36	①
Du et al[39]	Shandong province, China	January 23–February 15, 2020	Retrospective	14	6	8	Median age: 6.2 years Range: 0–16 years	14	①④
Wu et al[40]	Qdao Maternal and Child Health Hospital, China	January 20–February 27, 2020	Retrospective	74	44	30	Median age: 6.00 years Range: 0.10–15.08 years	74	①③④
Su et al[41]	Qilu Children's Hospital of Shandong University, Jinan, People's Republic of China	January 20–February 27, 2020	Retrospective	9	3	6	Average age: 4.5 years	9	①③
Foster et al[42]	Texas Children's Hospital	March 10–April 18, 2020	Retrospective	57	32	25	Median age: 10.7 years Range: 0.1–20.2 years	14	N
Zheng et al[43]	South China	January 21–February 29, 2020	Retrospective	52	28	24	Median age: 9 years Interquartile range: 4–12 years	51	N
De Ceano-Vivas et al[44]	Spain	March 11–April 9, 2020	Retrospective	58	37	21	Median age: 35.5 months Range: 3.3–146 months	40	①③④
Chao et al[45]	New York City	March 15–April 13, 2020	Retrospective	46	31	15	Median age: 13.1 years Interquartile range: 0.4–19.3 years	31	①③④
Mohammadi et al[46]	Urmia University of Medical Sciences, Urmia, Iran	January 25–March 25	Prospective observational study	27	10	17	Average age: 4.7 ± 4.16 years	27	①③④

① The distribution of lesion; ② lesion morphology; ③ change of lesion density; and ④ adjoint sign.
N = not mentioned.

Table 2

Summary of the meta-analysis results on CT image features.

Outcome indicators	Number of included studies	Sample size	Heterogeneity				Effect of mode	Meta-analysis results	
			P value	*Chi²*	*df*	*I²*		*R% (95% CI)*	*P value*
Distribution of lesions									
Rate of abnormal CT findings	37	1130	<.001	214.54	32	85.1%	Random	63.2% (55.8–70.6)	<.001
Multiple lung lobes lesions	12	184	.768	9.07	13	0	Fixed	65.1% (58.8–72.2)	<.001
Bilateral lung lesions	25	300	.169	25.91	20	22.8%	Fixed	61.5% (55.1–67.9)	<.001
Lesion density									
Crazy-paving pattern	10	183	<.001	0.93	3	0	Fixed	6.15% (1.5–10.8)	.01
Ground-glass opacities	30	780	<.001	251.45	29	88.5%	Random	39.5% (30.7–48.3)	<.001
Air bronchogram sign	7	121	.01	4.70	5	0.0%		11.2% (5.5–16.9)	<.001
Consolidation	24	594	<.001	157.17	15	90.5%	Random	24.1% (15.9–32.4)	<.001
Shape of lesions									
Nodules	9	160	.014	19.07	8	58.1%	Random	25.7% (15.6–35.9)	<.001
Patchy	13	323	<.001	73.12	11	85.0%	Random	36.8% (23.5–50.1)	<.001
Cord-like	6	129	.173	6.37	4	37.2%	Fixed	9.7% (2.4–17.0)	.009
Halo sign	7	124	.01	22.03	5	77.3%	Random	24.8% (8.5–41.2)	.003
Adjoint sign									
Pleural effusion	5	239	.05	16.76	5	70.2%	Random	9.1% (2.5–15.7)	.07

CI = confidence interval, CT = computed tomography.

2.3. Literature screening and data extraction

Two researchers independently searched and screened the articles and collected and cross-checked the data. If there was any dispute, it was resolved by a third researcher.

The inclusion criteria consisted of the following: research types: cohort study, case-control study, cross sectional studies, and case analysis; subjects: children with COVID-19; and observation index: imaging features of lung CT or high resolution CT, including lesion distribution, shape, and density change; and accompanying signs.

The exclusion criteria consisted of the following: repeated publications of the same research; short case reports; and incomplete or missing data analysis, without free or easy access to the data.

2.4. Quality evaluation of the included studies

This was a case series study that adhered to the National institute for Clinical excellence guidelines for quality evaluation.[9] The evaluation items were as follows: cases in the case series came from medical institutions at different levels and from various difference research centers; the research hypothesis or purpose was clearly described; clear reports were included in the exclusion criteria; measurement results were clearly defined; the collected data achieved the expected purpose; the patient recruitment period was clearly defined; the main findings were clearly described; and results were analyzed and reported in layers. One point was awarded for each item (maximum 8 points), with a total score ≥4 indicating high-quality research. Two researchers independently evaluated the quality and cross-checked the results.

2.5. Statistical analysis

A meta-analysis was performed using Stata12.0 software (STATA Corp, College Station, TX). First, the original ratio (R) was transformed by double arcsine to conform to a normal distribution, and then the transformed ratio (TR) was analyzed by meta-analysis. The final rate (r) and its 95% confidence interval (CI) were finally obtained by converting the results using the formula: $R=(\sin(tr/2))^2$. The meta-analysis was carried out using a random-effect model for all studies. The existence of publication bias was judged using the funnel chart, and the significance level was set as $\alpha=0.05$.

2.6. Ethical statement

This study was carried out in accordance with the recommendations and in the preferred reporting items for systematic reviews and meta-analyses guidelines. Hence, permission from the ethics committee or the institutional review board is not required.

3. Evidence synthesis

3.1. Literature screening process and results

A total of 2042 related articles were obtained, which were screened layer by layer. Ultimately, 37 studies were included in this report,[10–46] including 1747 children with COVID-19. Figure 1 shows the process and results of the literature screening.

3.2. Basic characteristics and quality evaluation results of the included studies

A total of 37 studies[10–46] were included (11 studies from outside China and 26 studies from China). The included studies were published from January 1, 2020 to August 10, 2020 (Table 1 summarizes the basic characteristics of the included studies; see Table S1, Supplemental Digital Content, http://links.lww.com/MD2/A466 for details). The quality scores of the included studies ranged from 4 to 8 points, indicating that all were high-quality studies (≥4 points, Table S2, Supplemental Digital Content, http://links.lww.com/MD2/A467).

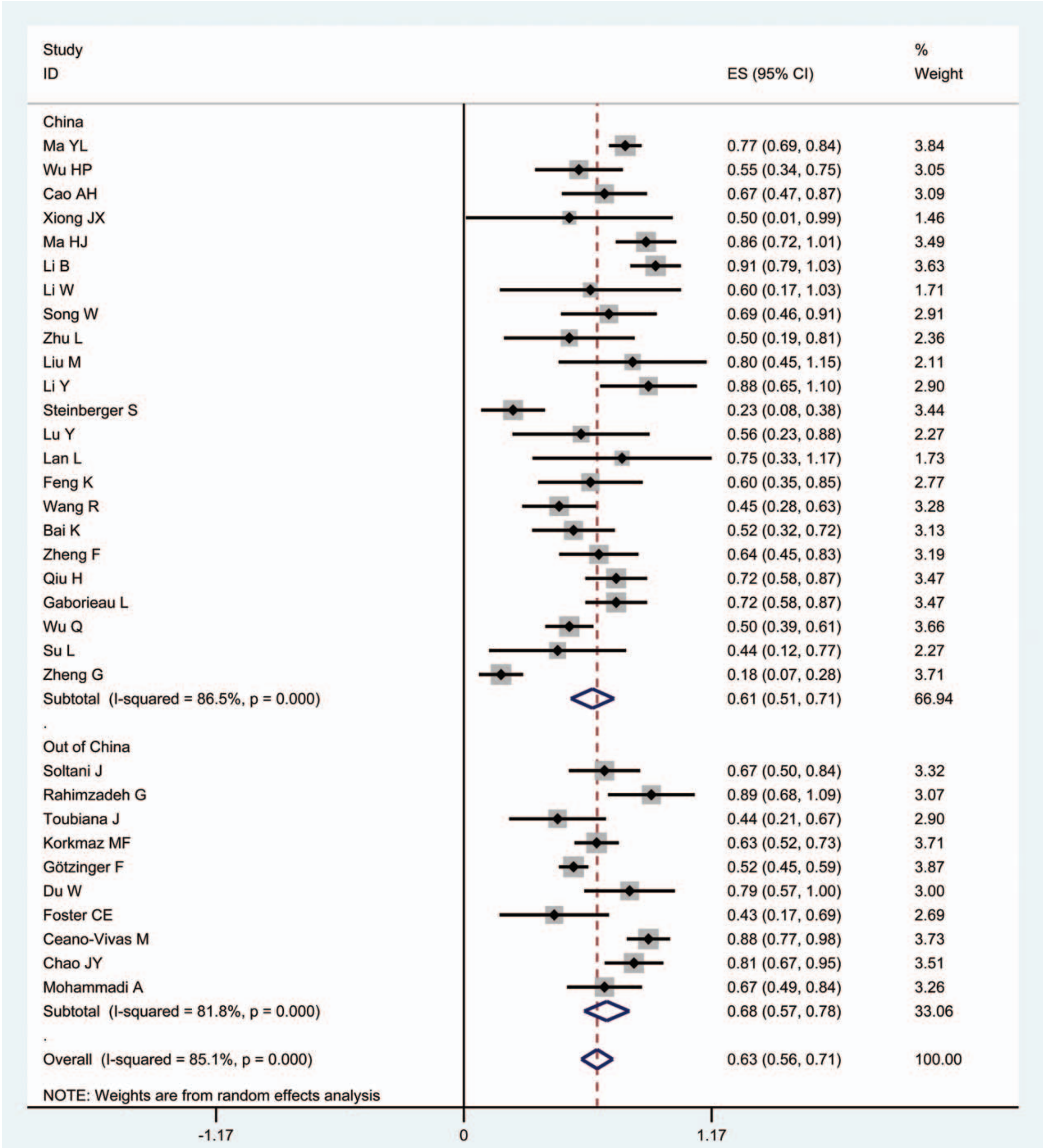

Figure 2. Forest plot of the abnormal pulmonary CT findings. CI = confidence interval, CT = computed tomography.

3.3. Meta-analysis results (Table 2)

3.3.1. Distribution of lesions. Meta-analysis of the random-effect model showed that the detection rate of abnormal lung CT findings was 63.2% (95% CI: 55.8%–70.6%), bilateral lung lesions was 61.5% (95% CI: 58.8%–72.2%), and multiple lung lobes lesions was 65.1% (95% CI: 55.1%–67.9%).

3.3.2. Lesion density. Meta-analysis of the random-effect model showed that the prevalence of nodules was 25.7% (95% CI: 15.6%–35.9%), patchy shadows was 36.8% (95% CI: 23.5%–50.1%), cord-like pattern was 9.7% (95% CI: 2.4%–17%), and halo signs was 24.8% (95% CI: 8.5%–10.8%).

3.3.3. Lesion shape. Meta-analysis of the random-effect model showed that the prevalence of a crazy-paving pattern was 6.15% (95% CI: 1.5%–10.8%), ground-glass opacities was 39.5% (95% CI: 30.7%–48.3%), air bronchogram signs was 11.2% (95% CI: 5.5%–16.98%), and consolidation was 24.1% (95% CI: 15.9%–41.2%).

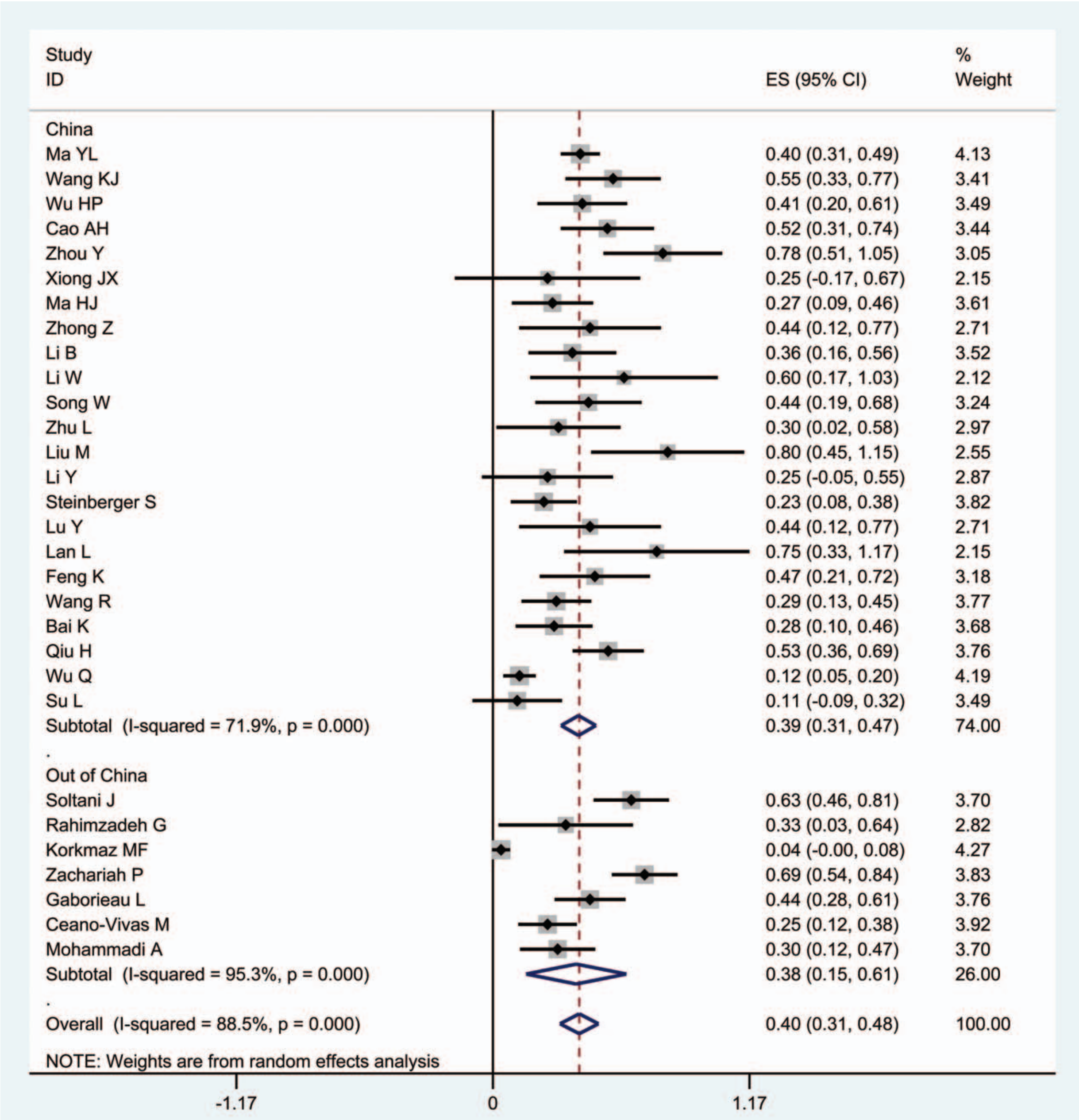

Figure 3. Forest plot of the ground-glass sample. CI = confidence interval.

3.3.4. Adjoint sign. Meta-analysis of the random-effect model showed that the prevalence of pleural effusion was 9.1% (95% CI: 2.5%–15.7%). Two articles in this study reported cases of white lung[10,16] and 1 article reported a case of pulmonary bullae.[15] A study outside China reported 2 cases of pneumothorax.[37]

3.3.5. Subgroup analysis. The heterogeneity of this study was large. To explore the source of heterogeneity, the study was classified according to the region where the study took place (China and non-China) and grouped by the rate of abnormal pulmonary CT findings and ground-glass sample index. The results of each subgroup were consistent with the overall results, and there was no significant difference between the heterogeneity of each subgroup and the whole group, indicating that regional differences were not the main source of heterogeneity (Figs. 2 and 3).

3.3.6. Sensitivity analysis. Sensitivity analysis was carried out for the observation indicators of abnormal changes in CT. After each study was eliminated successively, statistics were recombined, and the results showed no directional change, indicating relatively stable results (Fig. 4).

3.4. Publication bias

A funnel plot was drawn for the meta-analysis of abnormal lung CT indicators, and the results showed that the distribution at the left and right of each study point was asymmetrical (Fig. 5), the

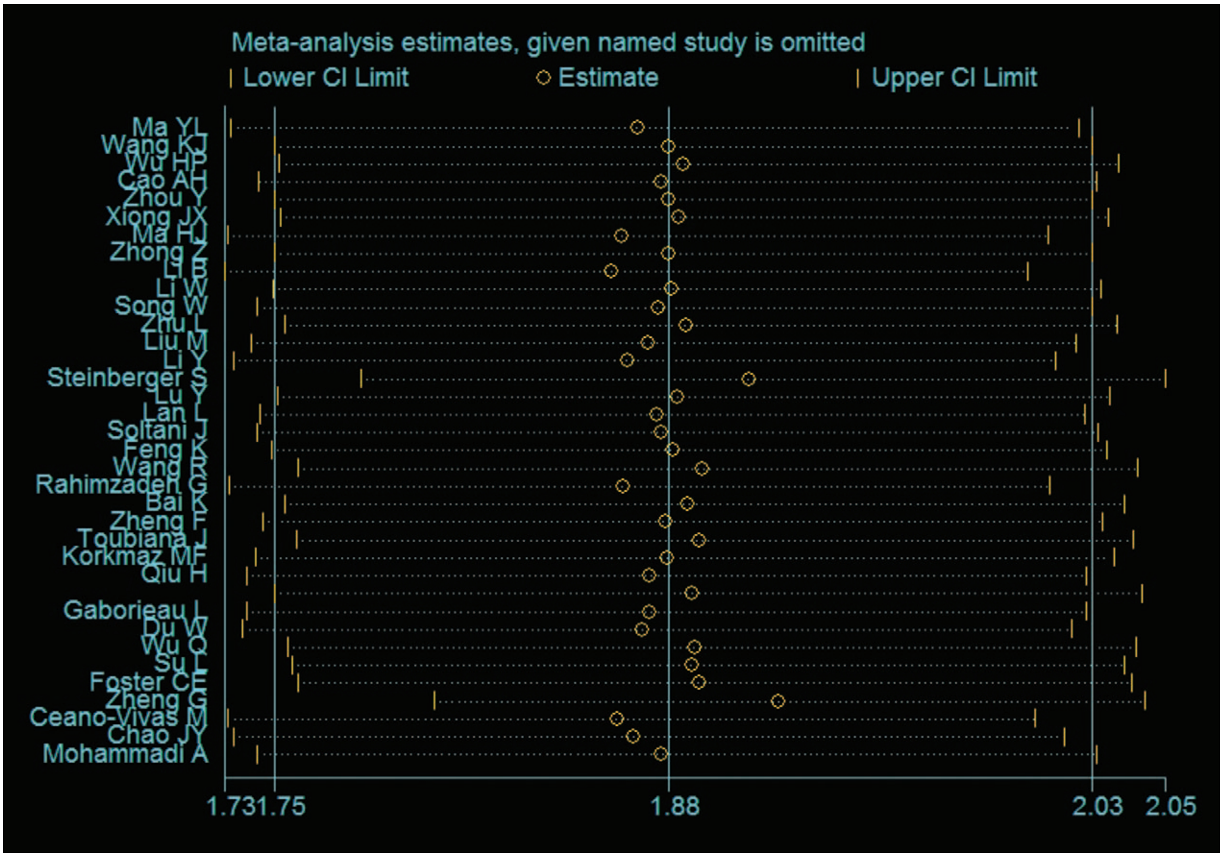

Figure 4. Sensitivity analysis of abnormal CT. CI = confidence interval, CT = computed tomography.

P values of Egger and Begg tests were .002 and .466, respectively, indicating that publication bias may exist in this study.

4. Discussion

Chest CT examination is a method used to diagnose COVID-19. CT manifestations of COVID-19 in adults mainly include patchy and segmental ground-glass density shadows in 1 or both lungs, or nodular shadows with surrounding ground-glass density shadows. It is mainly distributed around the vascular bundle, peripheral dorsal subpleural lung, and the lower lobes of both lungs, with the long axis parallel to the pleura. Air bronchogram and paving stone signs, among others, can also be observed.[47] In a systemic review, including 4121 cases of adult COVID-19 patients, it was found that the prevalence of typical ground-glass opacity was 68.1% (95% CI: 56.9%–78.2%) and that most patients had bilateral lung involvement (73.8%; 95% CI: 65.9%–81.1%) or lesions in multiple lung lobes (67.3%; 95% CI: 54.8%–78.7%).[48] Compared to adults, the current study found that the detection rate of abnormal CT findings in children was only 63.2% (95% CI: 55.8%–70.6%), which is similar to the study of the European Society of Paediatric Radiology Cardiothoracic Imaging Taskforce (64%).[49] Furthermore, the subgroup analysis showed that the basal rates of abnormal CT findings in and outside of China were 61% and 67.8%, respectively. While the incidence of typical ground-glass opacities was 39.5% (95% CI: 30.7%–48.3%), the subgroup analysis revealed that the incidences in and outside of China were 39.2% and 38.1%, respectively. Kumar et al[50] reported a ground glass shadow incidence of 40%, which was similar to the 39.5% reported in this study. However, Kumar et al[50] found that 55% patients had unilateral flash involvement, while this study was mainly affected by bilateral lung (61.5%). Generally, the pulmonary CT scans of children do not show typical findings as that of adults.

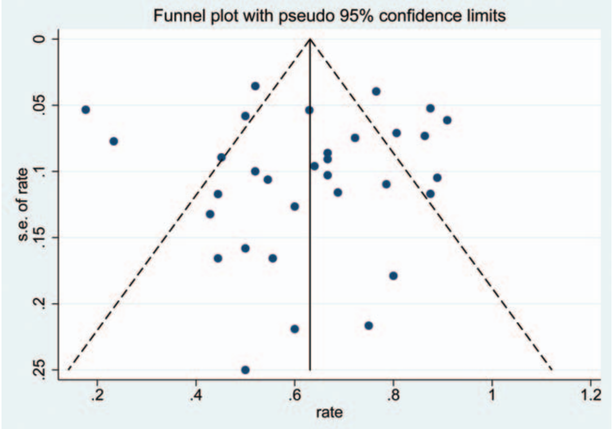

Figure 5. Funnel plot of CT anomaly rate. CT = computed tomography.

As for the CT examinations of asymptomatic children, Chinese scholar Lan[26] found and analyzed 4 cases with CT findings.

Thin-section CT revealed abnormalities in 3 patients, and 1 patient did not present with any abnormal CT findings. Unilateral lung involvement was observed in 2 patients, and 1 patient showed bilateral lung involvement. In total, 5 small lesions were identified, including ground-glass opacity (n=4) and consolidation (n=1). All lesions had ill-defined margins with peripheral distribution and a predilection for the lower lobes. At present, there is no large-scale study on the differences of lung CT findings between asymptomatic and symptomatic children.

Generally, the symptoms of children are relatively mild. In the current study, 2 cases of white lung were reported from Wuhan Children's Hospital; 1 article reported a case of pulmonary bullae.[14] In addition, a study outside China reported 2 cases of pneumothorax.[37] The symptoms of children are milder than those of adults, which may be related to differences in the angiotensin-converting enzyme 2 (ACE2) receptor. ACE2 is an important binding receptor for SARS-CoV-2.[5,10] The ACE2 receptor is still not quite mature in children and it also has reduced function than that in adults, making them less susceptible to SARS-CoV-2 binding. This also leads to a reduced SARS-CoV-2 load. In addition, the immune system of children is still in the phase of development; therefore, the intensity of the immune response (cytokine storm) is not as strong as that in adults, which reduces the damage to the body.[51]

Several limitations of our study need to be noted: Studies on children with COVID-19 are rare; there are 10 studies with less than 10 participants. Thus, the inspection efficiency may be insufficient. Most included studies were single-center studies; so, there may have been admission and selection biases. Most included studies were retrospective studies, which could not control for confounding factors. Reference,[10,21,37–38,44–46] the severity of the disease is inconsistent, which may lead to clinical heterogeneity. Last, as the pandemic spreads across the globe, additional data have become available for other regions not well represented in this study; therefore, more updated review and meta-analysis providing data for more regions of the world are needed. All these factors will affect the accuracy of the meta-analysis.

In conclusion, chest CT findings of children with COVID-19 are usually normal or slightly atypical; thus, the CT findings show low sensitivity and specificity. Children diagnosed with COVID-19 are mainly diagnosed through reverse-transcription polymerase chain reaction. For children with a high suspicion of COVID-19, imaging examination shows no abnormalities and conclusions should be drawn cautiously.

Author contributions

Ji-gan Wang and Yu-fang Mo conceived and designed the study. Ji-gan Wang, Yu-heng Su, Li-chuan Wang, and Qian-qiu Qin searched the literature and extracted data. Guang-bing Liu and Meng-Li performed statistical analyses. All authors wrote and reviewed the manuscript.

Conceptualization: Ji-Gan Wang.
Data curation: Ji-Gan Wang, Yu-Fang Mo, Meng Li.
Formal analysis: Ji-Gan Wang.
Methodology: Yu-Fang Mo, Guang-bing Liu.
Software: Yu-heng Su.
Validation: Yu-heng Su.
Visualization: Li-chuan Wang, Qian-qiu Qin.
Writing – original draft: Ji-Gan Wang, Yu-heng Su, Meng Li, Qian-qiu Qin.
Writing – review & editing: Ji-Gan Wang, Yu-heng Su, Li-chuan Wang.

References

[1] Li Q, Guan X, Wu P, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. N Engl J Med 2020;382:1199–207.
[2] Remuzzi A, Remuzzi G. COVID-19 and Italy: what next? Lancet 2020;2:10–3.
[3] Cucinotta D, Vanelli M. WHO declares COVID-19 a pandemic. Acta Biomed 2020;91:157–60.
[4] Chan JF, Yuan S, Kok KH, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. Lancet 2020;395:514–23.
[5] Liu H, Liu F, Li J, Zhang T, Wang D, Lan W. Clinical and CT imaging features of the COVID-19 pneumonia: focus on pregnant women and children. J Infect 2020;80:e7–13.
[6] Ai T, Yang Z, Hou H, et al. Correlation of chest CT and RT-PCR testing for coronavirus disease 2019 (COVID-19) in China: a report of 1014 cases. Radiology 2020;296:E32–40.
[7] Duan YN, Zhu YQ, Tang LL, Qin J. CT features of novel coronavirus pneumonia (COVID-19) in children. Eur Radiol 2020;30:4427–33.
[8] Dong Y, Mo X, Hu Y, et al. Epidemiology of COVID-19 among children in China. Pediatrics 2020;145:e20200702.
[9] Abraham C, Kelly MP, West R, Michie S. The UK National Institute for Health and Clinical Excellence public health guidance on behaviour change: a brief introduction. Psychol Health Med 2009;14:1–8.
[10] Ma YL, Xia SY, Wang M, et al. Analysis of clinical characteristics of 115 children infected by novel coronavirus. Chin J Contemp Pediatr 2020;22:290–3.
[11] Wang KJ, Xu L, Yin H, et al. Clinical features and CT imaging of children with covid-19. J Hubei Univ Med 2020;39:134–8.
[12] Wu HP, Li HF, Chen X, et al. Clinical analysis of covid-19 in 23 children under 18 years of age in Jiangxi province. Chin J Contemp Pediatr 2020;22:419–24.
[13] Cao AH, Duan CH, Qiu BP, et al. Epidemiology and clinical characteristics of children infected with virus from novel coronavirus in Shandong Province. J Shandong Univ (Health Sci) 2020;58:34–40.
[14] Zhou Y, Yang GD, Feng K, et al. Clinical characteristics and chest CT manifestations of covid-19 in infants and young children. Chin J Contemp Pediatr 2020;22:215–20.
[15] Xiong JX, Zhou CY, Zeng WB. CT findings of children with COVID-19. Chongqing Med 2020;49:2837–8.
[16] Ma HJ, Shao JB, Wang YJ, et al. High resolution CT findings of covid-19 children. Chin J Radiol 2020;310–3.
[17] Zhong Z, Xie XZ, Huang W, et al. Chest CT findings and clinical characteristics of children with covid-19 virus. J Central South Univ (Med Sci) 2020;45:236–42.
[18] Li B, Shen J, Li L, Yu C. Radiographic and clinical features of children with coronavirus disease (COVID-19) pneumonia. Indian Pediatr 2020;57:423–6.
[19] Li W, Cui H, Li K, Fang Y, Li S. Chest computed tomography in children with COVID-19 respiratory infection. Pediatr Radiol 2020; 50:796–9.
[20] Song W, Li J, Zou N, Guan W, Pan J, Xu W. Clinical features of pediatric patients with coronavirus disease (COVID-19). J Clin Virol 2020; 127:104377.
[21] Zhu L, Wang J, Huang R, et al. Clinical characteristics of a case series of children with coronavirus disease 2019. Pediatr Pulmonol 2020;55: 1430–2.
[22] Liu M, Song Z, Xiao K. High-resolution computed tomography manifestations of 5 pediatric patients with 2019 novel coronavirus. J Comput Assist Tomogr 2020;44:311–3.
[23] Li Y, Cao J, Zhang X, Liu G, Wu X, Wu B. Chest CT imaging characteristics of COVID-19 pneumonia in preschool children: a retrospective study. BMC Pediatr 2020;20:227.
[24] Steinberger S, Lin B, Bernheim A, et al. CT features of coronavirus disease (COVID-19) in 30 pediatric patients. Am J Roentgenol 2020;215:1–9.
[25] Lu Y, Wen H, Rong D, Zhou Z, Liu H. Clinical characteristics and radiological features of children infected with the 2019 novel coronavirus. Clin Radiol 2020;75:520–5.
[26] Lan L, Xu D, Xia C, Wang S, Yu M, Xu H. Early CT findings of coronavirus disease 2019 (COVID-19) in asymptomatic children: a single-center experience. Korean J Radiol 2020;21:919–24.

[27] Soltani J, Sedighi I, Shalchi Z, Sami G, Moradveisi B, Nahidi S. Pediatric coronavirus disease 2019 (COVID-19): an insight from west of Iran. North Clin Istanb 2020;7:284–91.
[28] Feng K, Yun YH, Wang LF, et al. CT image characteristics of children novel coronavirus 2019 infected with 15 cases. Chin J Pediatr 2020; 58:275–8.
[29] Wang R, Ju XL, Xie F, et al. Clinical analysis of 31 cases with novel coronavirus 2019 infection in 6 provinces (autonomous regions) in north China. Chin J Pediatr 2020;58:269–74.
[30] Rahimzadeh G, Ekrami Noghabi M, Elyaderani FK, et al. COVID-19 infection in Iranian children: a case series of 9 patients. J Pediatr Rev 2020;8:139–44.
[31] Bai K, Liu W, Liu C, et al. Clinical analysis of 25 COVID-19 infections in children. Pediatr Infect Dis J 2020;39:e100–3.
[32] Zheng F, Liao C, Fan QH, et al. Clinical characteristics of children with coronavirus disease 2019 in Hubei, China. Curr Med Sci 2020;40:275–80.
[33] Toubiana J, Poirault C, Corsia A, et al. Kawasaki-like multisystem inflammatory syndrome in children during the covid-19 pandemic in Paris, France: prospective observational study. BMJ 2020;369:m2094.
[34] Korkmaz MF, Türe E, Dorum BA, Kılıç ZB. The epidemiological and clinical characteristics of 81 children with COVID-19 in a pandemic hospital in Turkey: an observational cohort study. J Korean Med Sci 2020;35:e236.
[35] 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. Lancet Infect Dis 2020;20:689–96.
[36] Götzinger F, Santiago-García B, Noguera-Julián A, et al. COVID-19 in children and adolescents in Europe: a multinational, multicentre cohort study. Lancet Child Adolesc Health 2020;4:653–61.
[37] Zachariah P, Johnson CL, Halabi KC, et al. Epidemiology, clinical features, and disease severity in patients with coronavirus disease 2019 (COVID-19) in a children's hospital in New York City, New York. JAMA Pediatr 2020;174:e202430.
[38] Gaborieau L, Delestrain C, Bensaid P, et al. Epidemiology and clinical presentation of children hospitalized with SARS-CoV-2 infection in suburbs of Paris. J Clin Med 2020;9:E2227.
[39] Du W, Yu J, Wang H, et al. Clinical characteristics of COVID-19 in children compared with adults in Shandong Province, China. Infection 2020;48:445–52.
[40] Wu Q, Xing Y, Shi L, et al. Coinfection and other clinical characteristics of COVID-19 in children. Pediatrics 2020;146:e20200961.
[41] Su L, Ma X, Yu H, 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. Emerg Microbes Infect 2020; 9:707–13.
[42] Foster CE, Moulton EA, Munoz FM, et al. Coronavirus disease 2019 in children cared for at Texas Children's Hospital: initial clinical characteristics and outcomes. J Pediatric Infect Dis Soc 2020;9: 373–7.
[43] Zheng G, Wang B, Zhang H, et al. Clinical characteristics of acute respiratory syndrome with SARS-CoV-2 infection in children in South China. Pediatr Pulmonol 2020;55:2419–26.
[44] de Ceano-Vivas M, Martín-Espín I, Del Rosal T, et al. SARS-CoV-2 infection in ambulatory and hospitalised Spanish children. Arch Dis Child 2020;105:808–9.
[45] Chao JY, Derespina KR, Herold BC, et al. Clinical characteristics and outcomes of hospitalized and critically ill children and adolescents with coronavirus disease 2019 at a tertiary care medical center in New York City. J Pediatr 2020;223:14–9.e2.
[46] Mohammadi A, Mohebbi I, Khademvatani K, et al. Clinical and radiological characteristics of pediatric patients with COVID-19: focus on imaging findings. Jpn J Radiol 2020;38:987–92.
[47] Radiological diagnosis of COVID-19: expert recommendation of the Radiological Society of the Chinese Medical Association (first edition). Chin J Radiology 2020;4:279–85.
[48] Zhu J, Zhong Z, Li H, et al. CT imaging features of 4121 patients with COVID-19: a meta-analysis. J Med Virol 2020;92:891–902.
[49] Shelmerdine SC, Lovrenski J, Caro-Domínguez P, Toso S. Collaborators of the European Society of Paediatric Radiology Cardiothoracic Imaging TaskforceCoronavirus disease 2019 (COVID-19) in children: a systematic review of imaging findings. Pediatr Radiol 2020;50: 1217–30.
[50] Kumar J, Meena J, Yadav A, Yadav J. Radiological findings of COVID-19 in children: a systematic review and meta-analysis. J Trop Pediatr 2020;67: doi: 10.1093/tropej/fmaa045.
[51] South AM, Brady TM, Flynn JT. ACE2 (angiotensin-converting enzyme 2), COVID-19, and ACE inhibitor and Ang II (angiotensin II) receptor blocker use during the pandemic: the pediatric perspective. Hypertension 2020;76:16–22.