Original Article

Clinical characteristics of children with COVID-19: a rapid review and meta-analysis

Zijun Wang[1#], Qi Zhou[2#], Chenglin Wang[3,4,5#], Qianling Shi[2], Shuya Lu[6,7], Yanfang Ma[1], Xufei Luo[8], Yangqin Xun[1], Weiguo Li[3,4,5], Muna Baskota[3,4,5], Yinmei Yang[3,4,5], Hui Zhai[3,4,5], Toshio Fukuoka[9,10], Hyeong Sik Ahn[11,12], Myeong Soo Lee[13,14], Zhengxiu Luo[3,4,5], Enmei Liu[3,4,5], Yaolong Chen[1,15,16,17]; on behalf of COVID-19 Evidence and Recommendations Working Group

[1]Evidence-Based Medicine Center, School of Basic Medical Sciences, Lanzhou University, Lanzhou 730000, China; [2]The First School of Clinical Medicine, Lanzhou University, Lanzhou 730000, China; [3]Department of Respiratory Medicine, Children's Hospital of Chongqing Medical University, Chongqing 400014, China; [4]National Clinical Research Center for Child Health and Disorders, Ministry of Education Key Laboratory of Child Development and Disorders, China International Science and Technology Cooperation Base of Child Development and Critical Disorders, Children's Hospital of Chongqing Medical University, Chongqing 400014, China; [5]Chongqing Key Laboratory of Pediatrics, Chongqing 400014, China; [6]Department of Pediatric, Sichuan Provincial People's Hospital, University of Electronic Science and Technology of China, Chengdu 611731, China; [7]Chinese Academy of Sciences Sichuan Translational Medicine Research Hospital, Chengdu 610072, China; [8]School of Public Health, Lanzhou University, Lanzhou 730000, China; [9]Emergency and Critical Care Center, Department of General Medicine, Department of Research and Medical Education, Kurashiki Central Hospital, Kurashiki, Japan; [10]Advisory Committee in Cochrane Japan, Tokyo, Japan; [11]Department of Preventive Medicine, Korea University College of Medicine, Seoul, Korea; [12]Korea Cochrane Center, Seoul, Korea; [13]Korea Institute of Oriental Medicine, Daejeon, Korea; [14]University of Science and Technology, Daejeon, Korea; [15]Lanzhou University, an Affiliate of the Cochrane China Network, Lanzhou 730000, China; [16]Chinese GRADE Center, Lanzhou 730000, China; [17]Key Laboratory of Evidence Based Medicine and Knowledge Translation of Gansu Province, Lanzhou University, Lanzhou 730000, China

Contributions: (I) Conception and design: E Liu, Y Chen; (II) Administrative support: E Liu, Y Chen; (III) Provision of study materials or patients: E Liu; (IV) Collection and assembly of data: Z Wang, Q Zhou, C Wang, Q Shi, S Lu, Y Xun; (V) Data analysis and interpretation: Z Wang, Q Zhou, C Wang, Y Ma, X Luo; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

Correspondence to: Enmei Liu. Department of Respiratory Medicine, Children's Hospital of Chongqing Medical University, Chongqing 400014, China. Email: emliu186@126.com; Yaolong Chen. Evidence-Based Medicine Center, School of Basic Medical Sciences, Lanzhou University, Lanzhou 730000, China. Email: chenyaolong@lzu.edu.cn.

Background: Most guidelines on COVID-19 published so far include recommendations for patients regardless of age. Clinicians need a more accurate understanding of the clinical characteristics of children with COVID-19.

Methods: We searched studies reporting clinical characteristics in children with COVID-19 published until March 31, 2020. We screened the literature, extracted the data and evaluated the risk of bias and quality of evidence of the included studies. We combined some of the outcomes (symptoms) in a single-arm meta-analysis using a random-effects model.

Results: Our search retrieved 49 studies, including 25 case reports, 23 case series and one cohort study, with a total of 1,667 patients. Our meta-analysis showed that most children with COVID-19 have mild symptoms. Eighty-three percent of the children were within family clusters of cases, and 19% had no symptoms. At least 7% with digestive symptoms. The main symptoms of children were fever [48%, 95% confidence interval (CI): 39%, 56%] and cough (39%, 95% CI: 30%, 48%). The lymphocyte count was below normal level in only 15% (95% CI: 8%, 22%) of children which is different from adult patients. 66% (95% CI: 55%, 77%) of children had abnormal findings in CT imaging.

Conclusions: Most children with COVID-19 have only mild symptoms, and many children are asymptomatic. Fever and cough are the most common symptoms in children. Vomiting and diarrhea were not common in children. The lymphocyte count is usually within the normal range in children.

Keywords: Children; clinical characteristics; COVID-19; meta-analysis; rapid review

Submitted Apr 13, 2020. Accepted for publication Apr 26, 2020.
doi: 10.21037/atm-20-3302
View this article at: http://dx.doi.org/10.21037/atm-20-3302

Introduction

In December 2019, a previously unknown type of pneumonia broke out in Wuhan, China, which was later confirmed to be caused by a novel type of beta coronavirus, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). In February 2020, the World Health Organization (WHO) officially named the disease as "Coronavirus Disease 2019 (COVID-19)" (1). Like MERS-CoV and SARS-CoV, SARS-CoV-2 can also be transmitted between humans (2-5). Since the occurrence of COVID-19 case (6,7), the disease is spreading rapidly. WHO reassessed the potential impact of COVID-19 on global public health and subsequently declared COVID-19 as Public Health Emergency of International Concern (PHEIC) on January 30, 2020.

Research has proven that people of all ages are susceptible to SARS-CoV-2. The mean age of COVID-19 patients was 47 years, with 55% of the patients being between 15 and 49 years old. Only 9% of the patients were under 15 years old (8). For this reason, most of the guidelines published so far include recommendations for patients regardless of age, only a few recommendations are for children. Although the great majority of patients are adults, children's respiratory structural characteristics and immune response system differ essentially from those in adult (9-11), and the diagnostic criteria and management according to recommendations targeting adults may not be appropriate for children. Our study aims therefore to identify the clinical features of children with COVID-19, help clinicians to confirm and treat the suspected children as soon as possible, and provide support for the development of guidelines for COVID-19 in children. We present the following article in accordance with the PRISMA reporting checklist (available at http://dx.doi.org/10.21037/atm-20-3302).

Methods

Search strategy

We comprehensively searched the following electronic databases: Cochrane library, MEDLINE (via PubMed), Embase, Web of Science, China Biology Medicine disc (CBM), China National Knowledge Infrastructure (CNKI), and Wanfang Data from their inception until March 31, 2020 with the terms "2019-novel coronavirus", "SARS-CoV-2", "COVID-19", "2019-nCoV", "clinical features" and their derivatives. We also searched WHO, Chinese Center for Disease Control and Prevention (CCDC), National Health Commission of the People's Republic of China, USA National Institutes of Health Ongoing Trials Register (ClinicalTrials.gov), the ISRCTN registry, Google Scholar and the preprint servers medRxiv (https://www.medrxiv.org/), bioRxiv (https://www.biorxiv.org/) and SSRN (https://www.ssrn.com/index.cfm/en/). In addition, we searched the reference lists of the identified studies for further potential studies. The full search strategy can be found in Supplementary File I.

Inclusion and exclusion criteria

We included studies on children (aged <18 years) with COVID-19 that report clinical features of patients, such as symptoms, signs, laboratory examinations and imaging manifestations. Diagnosis of COVID-19 was based on the Novel Coronavirus Pneumonia Prevention and Control Program (7th edition) issued by the National Health and Health Committee of China (12) and surveillance case definitions for human infection with novel coronavirus (nCoV) Interim guidance v2 issued by WHO (13). We excluded *in vitro* studies, Traditional Chinese Medicine studies, conference abstracts, comments, letters, and

duplicates, and studies where we could not extract the data. We made no restrictions on language and publication status.

Study selection

Two reviewers (ZW and CW) selected the studies independently after first eliminating duplicates. The bibliographic software EndNote was used and any discrepancies were settled by discussion, consulting a third reviewer (QZ) if necessary. Before the formal selection, the reviewers searched a random sample of 50 citations. The reviewers screened first all titles and abstracts with the pre-defined criteria, and categorized the articles into three (eligible, not eligible, and unclear) groups. In the second step, full-texts of those potentially eligible or unclear studies were reviewed to identify the final inclusion. All the reasons for exclusion of ineligible studies were recorded, and the process of study selection was documented using a PRISMA flow diagram (14,15).

Data extraction

Two reviewers (QS and SL) extracted the data independently with a standardized data collection form, including: (I) basic information (e.g., first author); (II) symptoms; (III) routine blood tests (e.g., leucocyte count); (IV) blood biochemistry [e.g., alanine aminotransferase (ALT)]; (V) coagulation function (e.g., activated partial thromboplastin time); (VI) imaging findings (e.g., abnormal imaging). For dichotomous outcomes, we abstracted the number of events and total participants per group. For continuous outcomes, we abstracted means, standard deviations (SD), and the number of total participants in per group. Outcomes with no events were reported, but these were excluded from the meta-analysis. If means and SD were not reported, we calculated them from the reported indicators (16). If data were missing or reported in an unusable way, we excluded the study from the meta-analysis and report the findings descriptively.

Risk of bias assessment

Two reviewers (ZW and CW) assess the risk of bias in each study independently. Discrepancies were settled by discussion, consulting a third reviewer (QZ) if necessary. For randomized controlled trials (RCTs), we will assess the risk of bias independently using Cochrane risk-of-bias tool (17). It consists of seven domains, for each, we will grade as "Low", "Unclear", and "High". For nonrandomized controlled trials (nRCTs), ROBINS-I tool will be used (18). It consists of seven domains, for each, we will grade as "Low risk", "Moderate risk", "Serious risk", "Critical risk", and "No information". For case-control and cohort studies, the Newcastle-Ottawa Scale will be used (19). It consists of eight domains, for each, we will grade with stars. The more stars, the lower the risk of bias. For cross-sectional studies, we use a methodology evaluation tool recommended by Agency for Healthcare Research and Quality (AHRQ) (20). This tool assesses the quality of bias according to 11 criteria. And each criterion is answered by "Yes", "No" or "Unsure". For case reports and case series, we used a methodology evaluation tool recommended by National Institute for Health and Care Excellence (NICE) (21). The risk of bias is evaluated according to eight criteria. The results were summarized by scoring method, for the "Yes" items, the score was 1, and for the "No" items, the score was 0. The higher the total score, the lower the risk of bias.

Data synthesis

We summarized the results of the studies including less than nine patients and did meta-analysis of included studies that have at least nine patients. For dichotomous outcomes, we did a meta-analysis of proportions, reporting the effect size (ES) with 95% confidence intervals (CI). For continuous outcomes, we did a meta-analysis of continuous variable, calculating the ES with 95% CI. We described the results of the studies with patients that below nine. As clinical and methodological heterogeneity in the study design, characteristics of participants, interventions and outcome measures was expected, we used random-effects models (22). Two-sided P values <0.05 were considered statistically significant. Heterogeneity was defined as P values <0.10 and I^2>50%. All analyses were performed in STATA version 14.

Quality of the evidence assessment

Two reviewers (QZ and YX) assessed the quality of main evidence independently using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) tool. We produced a "Summary of Findings" table using the GRADE pro software (23,24). Direct evidence from RCTs is first set as high quality, and evidence from observational studies as low quality. Then initial quality can then be downgraded for five reasons (study

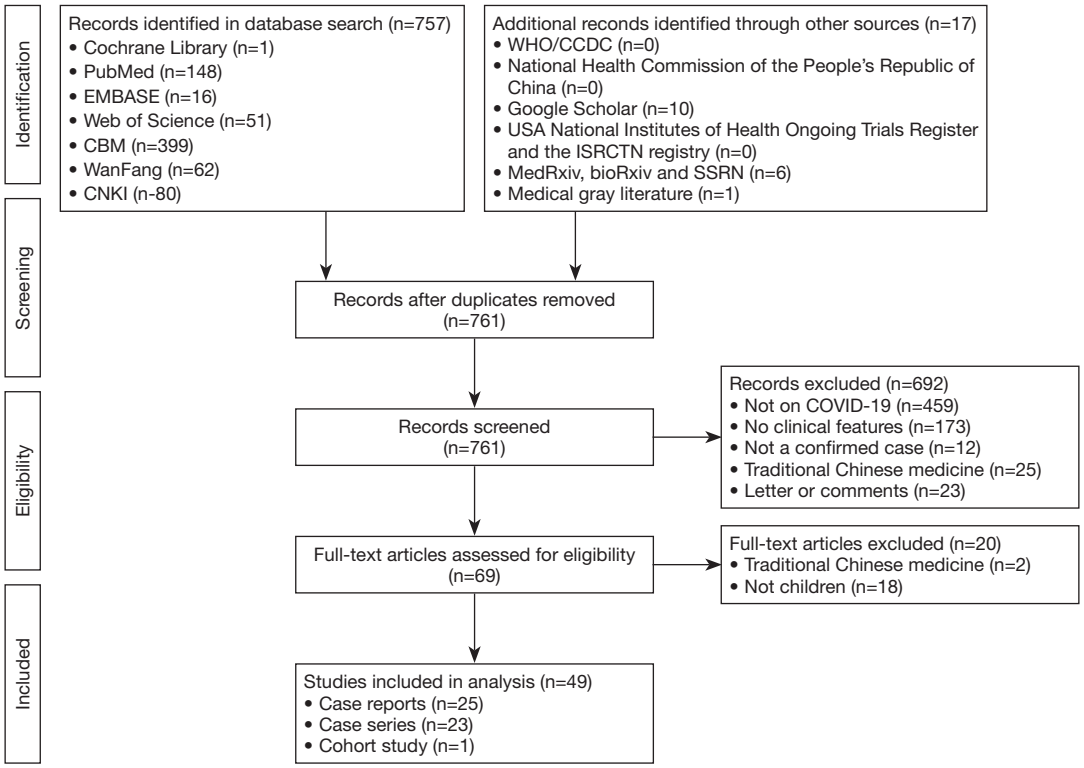

Figure 1 Flow diagram.

limitations, consistency of effect, imprecision, indirectness, and publication bias) and upgraded for three reasons (large magnitude of effect, dose-response relation and plausible confounders or biases) (25-30). Finally, the quality of main evidence can be classified as high, moderate, low, or very low, which reflects the extent to what we can be confident that the effect estimates are correct.

As COVID-19 is a PHEIC and the situation is evolving rapidly, our study was not registered in order to speed up the process (31).

Results

Study selection and characteristics

Our initial search retrieved 774 records (*Figure 1*). After removing duplicates, we screened the titles, abstracts and full texts, and 49 studies were finally included. The articles included 25 case reports, 23 case series and one cohort study. The studies included a total of 1,667 patients: 955 males and 712 females. Eighteen percent of children were aged less than 1 year. Most of the studies were carried out in China, including 17 studies from Hubei (*Table 1*). One study was from Singapore, one from Korea, one from Vietnam and one from Iran. The results on risk of bias are reported in Supplementary File II, and quality of the evidence in Supplementary File III.

Symptoms and imaging results

All of the included studies reported the symptoms of children with COVID-19. The results showed that 83% (95% CI: 78%, 88%) of the cases had likely acquired the infection from their family members with COVID-19. Ninety-four percent (95% CI: 90%, 98%) of children were mild cases and 3% (95% CI: 2%, 4%) were severe case. Among the children with severe symptoms that reported symptom clearly, 9 children have comorbidity, 10 children have gastrointestinal symptoms and 4 children have concurrent infection. Only two children were dead that has been reported in our included studies (46,65). The main symptoms were fever [48% (95% CI: 39%, 56%)], cough [39% (95% CI: 30%, 48%)]. Thirty percent (95% CI: 18%, 42%) of children had both cough and fever. Seven percent (95% CI: 5%, 9%) and 6% (95% CI: 4%, 9%) of cases had

Table 1 Characteristics of included studies

First author	Study location	Number			Age (year)	Study design
		All	M	F		
Deng 2020 (32)	Xian	2	1	1	8.0±7.1	Case report
Cai 2020 (33)	Shanghai	1	1	0	7	Case report
Zhang 2020 (34)	Hunan	1	0	1	0.2 (0.1, 0.3)	Case report
Wei 2020 (35)	Hubei	9	2	7	0.58 (0.28, 0.79)	Case series
Chen 2020 (36)	Hubei	1	1	0	1.1	Case report
Zeng 2020 (37)	Hubei	1	1	0	0	Case report
Feng 2020 (38)	Shenzhen	15	5	10	8.0±2.9	Case series
Wang 2020 (39)	Hubei	1	1	0	5.6	Case report
Quan 2020 (40)	Liaoning	1	0	1	4	Case report
Xiong 2020 (41)	Chongqing	2	1	1	5.2/5.2	Case report
Cai 2020 (42)	Shanghai	10	4	6	6.5 (4.0, 9.0)	Case series
Wang 2020 (43)	Xian	31	15	16	7.9±4.0	Case series
Tang 2020 (44)	Shenzhen	26	9	17	6.90±0.70	Case series
Liu 2020 (45)	Hubei	6	2	4	3.0 (3.0, 4.0)	Case report
Lu 2020 (46)	Hubei	171	104	67	7.1±2.8	Case series
Ma 2020 (47)[†]	Hubei	50	28	22	2.5 (0.9, 7.0)	Case series
Zhao 2020 (48)	Zhejiang	1	1	0	13	Case report
Li 2020 (49)	Hubei	30	18	12	6.5±3.4	Case series
Zhang 2020 (50)	Shandong	10	3	7	5.7±4.2	Case series
Zhang 2020 (51)	Hunan	2	0	2	1.2/1.2	Case report
Liu 2020 (52)	Hubei	1	1	0	9	Case report
Xiao 2020 (53)	Chongqing	1	0	1	7.83	Case report
Xu 2020 (54)	Chongqing	32	17	15	9.0±4.7	Case series
Chan 2020 (55)	Hong Kong	1	1	0	10	Case report
Kam 2020 (56)	Singapore	1	1	0	0.5	Case report
Park 2020 (57)	Korea	1	0	1	10	Case report
Du 2020 (58)	Shandong	14	6	8	7.1±4.7	Case series
Liu 2020 (59)	Shanghai	4	2	2	3.8±4.1	Case report
Wang 2020 (60)	Hubei	1	1	0	0	Case report
Rahimzadeh 2020 (61)	Iran	9	6	3	5.0 (3.5, 5.5)	Case series
Ji 2020 (62)	Beijing	2	2	0	9/15	Case report
Xu 2020 (63)	Guangzhou	10	6	4	6.6 (1.8, 13.7)	Case series
Xia 2020 (64)	Hubei	20	13	7	4.7±3.9	Case series
Dong 2020 (65)	Shanghai	731	420	311	10 (NR)	Case series

Table 1 (*continued*)

Table 1 (*continued*)

First author	Study location	Number			Age (year)	Study design
		All	M	F		
Xing 2020 (66)	Hong Kong	3	2	1	1.5/2.5/3.6	Case report
Yu 2020 (67)	Hubei	82	51	31	NR [0–16]	Case series
Liu 2020 (68)	Hubei	91	56	35	NA	Case series
Ma 2020 (69)	Hubei	115	73	42	NA	Case series
Qian 2020 (70)	Zhejiang	2	0	2	1.1	Case report
Qiu 2020 (71)	Zhejiang	36	23	13	8.3±3.5	Cohort study
Zhang 2020 (72)	Hubei	25	14	11	3.0 (2.0, 9.0)	Case series
Sun 2020 (73)	Hubei	8	6	2	5.0 (1.0, 13.7)	Case report
Dong 2020 (74)	Hubei	2	2	0	3/2.3	Case report
Wu 2020 (75)	Shandong	74	44	30	6.0 (0.1, 15.1)	Case series
Su 2020 (76)	Shandong	9	3	6	3.6 (1.8, 6.8)	Case series
Le 2020 (77)	Vietnam	1	0	1	0.3	Case report
Zhong 2020 (78)	Hunan	9	4	5	8 (1.5, 10.0)	Case series
Yang 2020 (79)	Shandong	10	3	7	4 (2, 8)	Case series
Tang 2020 (80)	Zhejiang	1	1	0	10	Case report

Ages were reported either as mean ± SD, or median (interquartile range), or single year. †, This article once has been retracted and republished by SSRN, now the data was updated with the new article. SD, standard deviation; NR, not report; NA, not applicable.

diarrhea and nausea/vomiting. The proportion of children with more than one symptom was 35% (95% CI: 21%, 48%), and 19% (95% CI: 14%, 23%) of all children were asymptomatic.

Forty-two studies reported the imaging features of children with COVID-19, including 19 case series and 23 case reports. Sixty-six percent (95% CI: 55%, 77%) had abnormal imaging. Thirty-five percent (95% CI: 26%, 44%) of children had ground-glass opacity.

More information can be found in *Table 2* and Supplementary File IV.

Laboratory results

Seventeen case series reported the results of routine blood tests. The mean leucocyte count in children was 6.25×10^9/L (95% CI: 5.97, 6.54). Fifteen percent (95% CI: 4%, 26%) of cases had leucocyte count above the normal range and 28% (95% CI: 17%, 38%) of cases below the normal range. The mean lymphocyte count in children was 2.84×10^9/L (95% CI: 2.55, 3.13). Lymphocyte count was elevated in 41% (95% CI: 2%, 80%) and below normal in 15% (95% CI: 8%, 22%) of children.

Eighteen case series reported the results of blood biochemistry tests. The mean value of ALT was 20.46 U/L (95% CI: 14.51, 26.41), and 11% (95% CI: 8%, 14%) of cases had elevated ALT values. The mean value of aspartate aminotransferase (AST) was 32.04 U/L (95% CI: 30.25, 33.83), and 15% (95% CI: 9%, 21%) of cases had elevated AST values. The mean value of C-reactive protein (CRP) was 5.05 mg/L (95% CI: 1.86, 8.24), and CRP was elevated in 22% (95% CI: 15%, 28%) of the children.

Nine case series reported coagulation function test, the mean value of D-dimer was 0.33 mg/L (95% CI: 0.17, 0.49) in studies of children with COVID-19. Fifteen percent (95% CI: 7%, 22%) of cases above the normal range of D-dimer value.

More information can be found in *Table 3* and Supplementary IV.

Table 2 Symptoms and imaging results of patients with COVID-19

Variable	ES	I^2 (%)	P value
The overall symptoms			
No Symptom	19% (14%, 23%)	70.7	<0.10
Mild symptom	94% (90%, 98%)	89.9	<0.10
Severe symptom	3% (2%, 4%)	22.5	0.24
More than one sign or symptom	35% (21%, 48%)	80.8	<0.10
Specific symptoms			
Fever	48% (39%, 56%)	85.7	<0.10
Cough	39% (30%, 48%)	84.4	<0.10
Fever and cough	30% (18%, 42%)	67.4	<0.10
Sputum production	19% (0%, 44%)	97.5	<0.10
Rhinorrhea	9% (6%, 12%)	0.0	0.64
Shortness of breath/dyspnea	9% (0%, 19%)	91.8	<0.10
Myalgia or fatigue	8% (5%, 12%)	56.7	<0.10
Diarrhea	7% (5%, 9%)	0.0	0.62
Nausea or vomiting	6% (4%, 9%)	0.0	1.00
Nasal obstruction	6% (3%, 9%)	0.0	0.59
Sore throat	6% (2%, 10%)	35.2	0.13
Headache	4% (1%, 6%)	0.0	0.61
Imaging findings			
Abnormal	66% (55%, 77%)	89.6	<0.10
Unilateral pneumonia	31% (20%, 43%)	81.5	<0.10
Bilateral pneumonia	28% (20%, 36%)	81.3	<0.10
Ground-glass opacity	35% (26%, 44%)	84.7	<0.10

ES, effect size.

Discussion

Principal findings

Children had on average milder symptoms, with many children having even no symptoms. Most children infected with COVID-19 were exposed through family clusters. About half of children present with fever or cough, and about one-third of children with both fever and cough. Only a small minority of children had vomiting or diarrhea as initial symptoms. Leucocyte and lymphocyte counts are often in normal or above the normal range in children with COVID-19. Abnormalities in CT imaging were found in more than half of the children, the most common being ground-glass opacity in unilateral lung.

The course of COVID-19 in children can be characterized by mild illness and no symptoms. According to a study by the CCDC, as of February 11, 2020, 81% of all patients with COVID-19 showed only mild symptoms (81). However, although the disease was less severe in the majority of adults (51–74%) (82-84), 26–32% of adults were still committed to ICU, and had often basic diseases such as hypertension or diabetes (85-87). In contrast, we found only 3% report of children with severe illness. The CCDC also pointed out that 889 (1%) patients with COVID-19 were asymptomatic (81); in our study, about 19% of children were completely asymptomatic, which is higher than the average level of the whole patient significantly. A study of asymptomatic infections with

Table 3 Laboratory results of children with COVID-19

Laboratory results	ES	I^2 (%)	P value
Routine blood values			
Leucocytes ($\times10^9$/L)	6.60 (6.19, 7.01)	65.9	<0.10
Above normal range	15% (4%, 26%)	77.3	<0.10
Below normal range	28% (17%, 39%)	85.7	<0.10
Lymphocytes ($\times10^9$/L)	2.76 (2.47, 3.05)	75.7	<0.10
Above normal range	41% (3%, 78%)	98.3	<0.10
Below normal range	15% (8%, 22%)	79.9	<0.10
Neutrophils ($\times10^9$/L)	2.70 (2.10, 3.31)	93.8	<0.10
Above normal range	23% (0%, 48%)	85.8	<0.10
Below normal range	24% (4%, 44%)	58.5	<0.10
Platelets ($\times10^9$/L)	257.09 (251.06, 263.13)	0.0	0.88
Above normal range	10% (3%, 17%)	45.5	0.14
Below normal range	7% (0%, 19%)	84.4	<0.10
Hemoglobin (g/L)	127.61 (123.80, 131.41)	87.4	<0.10
Above normal range	13% (4%, 22%)	58.4	<0.10
Below normal range	7% (0%, 14%)	53.6	0.12
Blood biochemistry			
Albumin (g/L)	45.30 (45.13, 45.47)	0.0	0.70
Below normal range	35% (25%, 45%)	0.0	0.33
Alanine aminotransferase (U/L)	20.46 (14.51, 26.41)	96.9	<0.10
Above normal range	11% (8%, 14%)	0.0	0.72
Aspartate aminotransferase (U/L)	32.04 (30.25, 33.83)	49.2	<0.10
Above normal range	15% (9%, 21%)	45.8	<0.10
Total bilirubin (μmol/L)	8.14 (1.45, 14.82)	97.5	<0.10
Above normal range	3% (0%, 6%)	NA	NA
Blood urea nitrogen (mmol/L)	3.81 (3.43, 4.18)	0.0	0.56
Above normal range	12% (0%, 33%)	94.9	<0.10
Below normal range	14% (0%, 35%)	57.6	0.13
Creatinine (μmol/L)	41.60 (32.98, 50.22)	95.6	<0.10
Above normal range	12% (0%, 33%)	94.9	<0.10
Below normal range	8% (3%, 14%)	0.0	0.59
Creatine kinase (U/L)	104.37 (95.66, 113.08)	56.6	0.10
Above normal range	13% (0%, 38%)	77.0	<0.10
Lactate dehydrogenase (U/L)	264.43 (241.85, 287.02)	98.1	<0.10
Above normal range	38% (25%, 51%)	72.9	<0.10

Table 3 (*continued*)

Table 3 (*continued*)

Laboratory results	ES	I^2 (%)	P value
Below normal range	11% (0%, 32%)	NA	NA
Myoglobin (μg/L)	15.33 (11.18, 19.48)	NA	NA
Procalcitonin (g/L)	0.06 (0.00, 0.16)	0.0	1.00
Above normal range	44% (20%, 69%)	98.0	<0.10
CRP (mg/L)	5.05 (1.86, 8.24)	86.9	<0.10
Above normal range	22% (15%, 29%)	71.3	<0.10
Coagulation function			
Activated partial thromboplastin time (s)	37.59 (28.69, 46.48)	96.4	<0.10
Increased	11% (5%, 18%)	0.0	0.72
Decreased	4% (0%, 8%)	NA	NA
Prothrombin time (s)	12.25 (11.30, 13.20)	99.0	<0.10
Increased	2% (0%, 4%)	0.0	0.42
Decreased	2% (0%, 6%)	NA	NA
D-dimer (mg/L)	0.33 (0.17, 0.49)	0.0	0.98
Increased	15% (7%, 22%)	38.4	0.17

ES, effect size; NA, not applicable.

COVID-19 also showed that 29.2% of cases showed normal CT image and had no symptoms during hospitalization. What's more, these cases were younger (median age: 14.0 years; P=0.012) than the rest (88). Of children with COVID-19, 83% had other family members infected. The majority of asymptomatic children in family clusters were confirmed after a positive nucleic acid test, which was conducted because of the close contact to infected family members. It seems that family cluster in children were more likely to be tested than adults. So, we suspect whether asymptomatic children are really asymptomatic or are still in the incubation period. Another explanation could be that only symptomatic cases transmit; So, adults without symptoms are seldom diagnosed, while children without symptoms (who had not that many any other contacts during the holiday season than their family members) get diagnosed anyway because of the obvious exposure.

The diagnosis of suspected cases in children needs comprehensive consideration. Fever and cough were the main symptoms in patients with COVID-19, which is reported by the most of current guidelines and recommendations (12,89-92). Although fever and cough also the first two symptom of children. When compared with adults, fever and cough occurred only in 48% and 39% of children, respectively. The rates of fever and cough in adults are up to 98% (87) and 87% (83), which indicates that fever and cough in children are not as common as in adults. Compared with children infected with SARS, MERS and other viral diseases (93,94), there are no specific symptoms in children with COVID-19 that could help to diagnose the disease accurately. Therefore, detection methods are particularly important for the diagnosis of COVID-19. Chinese National Health Commission also pointed out that fever and/or respiratory symptoms, imaging features indicating of pneumonia, leukocyte and lymphocyte counts characteristics in the early stage, and epidemiological history should be comprehensively used to determine suspected cases. After that, RT-PCR, sequencing or specific antibody were used to make a definite diagnosis (12).

Attention should be paid to the children with COVID-19 who start with gastrointestinal symptoms. Although gastrointestinal symptoms such as nausea, vomiting and diarrhea are less common in children with COVID-19, recent studies have SARS-CoV-2 in the feces of patients (95,96) and a study showed that some children persistently tested positive on rectal swabs even after nasopharyngeal testing was negative, raising the possibility of fecal-oral

transmission (63). According to one study, diarrhea was the first symptom in three out of 31 children (87). Moreover, three of the eight children with severe cases of COVID-19 that reported symptom clearly had gastrointestinal symptoms, one of them started with gastrointestinal symptoms, without any obvious respiratory tract infection in the early stage (36). In addition, comorbidity cannot be ignored either. Our results showed that half of these eight children with severe cases had other diseases, including two with intussusception and one of them was dead (46). Similarly, a study of children with MERS also suggest that serious illness can occur in children with underlying disease (94). Although there is no evidence that gastrointestinal symptoms and comorbidity in children are related to the severity of the disease, clinicians should pay attention to the gastrointestinal symptoms and comorbidity in the process of diagnosing children with COVID-19 and apply real-time monitoring and protection.

Abnormal CT imaging was less common in children with COVID-19 than adults, but the imaging findings were similar in children and adults. Unilateral pneumonia is common in children with COVID-19, and the main change in imaging is ground-glass opacity. However, bilateral pneumonia is more common in adults, and the main change in imaging is also ground-glass opacity (85,86). One guideline (92) pointed out that there were multiple small patch shadows and interstitial changes in the early stages of the disease in adults, especially in the extrapulmonary zone in chest imaging. Furthermore, multiple ground-glass opacity or infiltrative shadows may develop in both lungs. In severe cases, pulmonary consolidation may occur, and pleural effusion is rare. An analysis of CT features in children with COVID-19 showed that in 15 cases, inflammatory infiltration was found in the chest CT imaging during initial diagnosis and reexamination. Most inflammatory infiltrations were manifested as small nodular ground-glass opacities, and multiple lobe segments were less involved. Multiple lobe segments were involved in only one case, and the imaging changes were not typical in the advanced stage as well (38). These findings suggest that pulmonary inflammation in children is mild and localized.

The results of laboratory tests of children with COVID-19 were more often within the normal range than those of adults. The leukocyte count of children with COVID-19 was usually normal or below the normal range. The lymphocyte count was generally normal or above the normal range, and only 15% of cases were below the normal range. While for adults, the leukocyte count was usually normal or above the normal range, and the lymphocyte count were mostly below the normal range (35–63%) (85,86). It can be seen that there were significant differences in routine blood values between adults and children. However, some published COVID-19 guidelines and consensus for children consider a reduction in lymphocyte count as one of the factors for diagnosing suspected cases (89-91). Our study demonstrates that guidelines for children should not be formulated in full accordance with adult standards, otherwise true cases may be missed. Other laboratory tests, including liver and renal function, CRP, procalcitonin (PCT) and coagulation tests, most indicators in children tend to be normal. Although 35% of children with COVID-19 had albumin below the normal range, 38% of cases had lactate dehydrogenase above the normal range, and 22% of cases had CRP above the normal range, which were the most significant changes of children, the rate of changes was still much lower than in adults (86). This result suggests that majority of children with COVID-19 have laboratory results within the normal range, but close clinical monitoring should still be observed.

Most of the existing systematic reviews on characteristics of patients with COVID-19 are based on adult patients or patients regardless of age (97-102). Two of these compared the differences between children and adult patients (97,98). Only one review reported the clinical characteristics of children with COVID-19 at present (103). All reviews that considered children had similar outcomes: for example, children had milder symptoms than adults, some children had no symptoms, and lymphopenia in children did not occur as often as in adults. But our rapid review has included 49 studies of children patients, which is more than most of these reviews together. In contrast to another systematic review of children with COVID-19 (103), we included studies not only China but also from other countries such as Singapore, which were published in Chinese and English. Moreover, we conducted a meta-analysis whereas the previous study only did a systematic literature review.

Strengths and limitations

This rapid review has several strengths. First, although this is not the first systemic review about the clinical characteristics of children with COVID-19, but is to our knowledge the first to combine the results with meta-analysis and GRADE evaluation of the quality of main evidence, which is of great importance for clinicians to diagnose and treat children rapidly. Second, our study points out the loopholes in some

current guidance documents that suggest the diagnosis of suspected cases—also in children—based on the lymphocyte count. Third, as a rapid review, this study summarizes the latest published information on clinical cases, which provides relatively high-quality evidence for the formulation of clinical practice guidelines in the rapidly evolving public health emergency situation and helps policy-makers to make evidence-based decisions quickly (104).

Our study has also some limitations. First, due to the rapid fermentation of the public health emergency and new cases emerging continuously, the findings of this review may get outdates relatively soon. Second, cannot be sure if some cases were included in multiple studies. Third, at present, there is no unified definition for clinical classification of the severity of COVID-19, so we had to combine light, mild and moderate disease into one category (mild), while severe and critical cases were both considered as severe cases.

Future implications

The researchers should aim to conduct more targeted studies on COVID-19 in specific subpopulations. Policy makers should develop accurate guidelines for both children and adults. Clinical practitioners should pay attention on the specific characteristics of different patient populations to improve the accuracy of diagnosis and treatment.

Conclusions

Children with COVID-19 are more common to have only mild symptoms, and many children are even completely asymptomatic. Fever and cough are the main symptoms of COVID-19 in both children. Vomiting and diarrhea occurring less frequently in children. Ground-glass opacity is the most common CT imaging of children. Whereas adults tend to have elevated lymphocyte count at the beginning of the disease, in children the lymphocytes were usually within the normal range. As the characteristics of COVID-19 differ between adults and children in multiple ways, specific criteria for the diagnosis and treatment of COVID-19 in children are urgently needed.

Acknowledgments

We thank Janne Estill, Institute of Global Health of University of Geneva for providing guidance and comments for our review. We thank all the authors for their wonderful collaboration.

Funding: This work was supported by grants from National Clinical Research Center for Child Health and Disorders (Children's Hospital of Chongqing Medical University, Chongqing, China) (grant number NCRCCHD-2020-EP-01) to EL; Special Fund for Key Research and Development Projects in Gansu Province in 2020, to YC; the Fourth Batch of "Special Project of Science and Technology for Emergency Response to COVID-19" of Chongqing Science and Technology Bureau, to EL; special funding for prevention and control of emergency of COVID-19 from Key Laboratory of Evidence Based Medicine and Knowledge Translation of Gansu Province (grant number No. GSEBMKT-2020YJ01), to YC; The Fundamental Research Funds for the Central Universities (lzujbky-2020-sp14), to YC.

Footnote

Reporting Checklist: The authors have completed the PRISMA reporting checklist. Available at http://dx.doi.org/10.21037/atm-20-3302

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/atm-20-3302). MSL serves as the unpaid editorial board member of *Annals of Translational Medicine* from Nov 2019 to Oct 2021. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. World Health Organization. WHO Director-General's remarks at the media briefing on 2019-nCoV on 11

February 2020. 2020. Available online: https://www.who.int/dg/speeches/detail/who-director-general-s-remarks-at-the-media-briefing-on-2019-ncov-on-11-february-2020
2. Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med 2020;382:727-33.
3. Lu R, Zhao X, Li J, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet 2020;395:565-74.
4. 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.
5. Yu P, Zhu J, Zhang Z, et al. A familial cluster of infection associated with the 2019 novel coronavirus indicating potential person-to-person transmission during the incubation period. J Infect Dis 2020. doi: 10.1093/infdis/jiaa077.
6. Lu H, Stratton CW, Tang YW. Outbreak of pneumonia of unknown etiology in Wuhan, China: The mystery and the miracle. J Med Virol 2020;92:401-2.
7. Bogoch II, Watts A, Thomas-Bachli A, et al. Potential for global spread of a novel coronavirus from China. J Travel Med 2020. doi: 10.1093/jtm/taaa011.
8. Wu J, Wu X, Zeng W, et al. Chest CT findings in patients with corona virus disease 2019 and its relationship with clinical features. Invest Radiol 2020;55:257-61.
9. Shen K, Yang Y, Wang T, et al. Diagnosis, treatment, and prevention of 2019 novel coronavirus infection in children: experts' consensus statement. World J Pediatr 2020. [Epub ahead of print].
10. Shen KL, Yang YH. Diagnosis and treatment of 2019 novel coronavirus infection in children: a pressing issue. World J Pediatr 2020. [Epub ahead of print].
11. Chen ZM, Fu JF, Shu Q. New coronavirus: new challenges for pediatricians. World J Pediatr 2020. [Epub ahead of print].
12. National Health Commission of the People's Republic of China. The novel coronavirus pneumonia diagnosis and treatment plan (trial version 7). 2020. Available online: http://www.nhc.gov.cn/yzygj/s7653p/202003/46c9294a7dfe4cef80dc7f5912eb1989.shtml
13. World Health Organization. Global Surveillance for human infection with coronavirus disease (COVID-19). 2020. Available online: https://www.who.int/publications-detail/global-surveillance-for-human-infection-with-novel-coronavirus-(2019-ncov)
14. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. PLoS Med 2009;6:e1000100.
15. Tian J, Zhang J, Ge L, et al. The methodological and reporting quality of systematic reviews from China and the USA are similar. J Clin Epidemiol 2017;85:50-8.
16. Wan X, Wang W, Liu J, et al. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. BMC Med Res Methodol 2014;14:135.
17. Higgins JPT, Altman DG, Gotzsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ 2011;343:d5928.
18. Sterne JAC, Hernán MA, Reeves BC, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. BMJ 2016;355:i4919.
19. Wells G, Shea B, O'Connell D, et al. Newcastle–Ottawa Quality Assessment Scale--Case Control Studies. Available online: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp
20. Rostom A, Dubé C, Cranney A, et al. Celiac Disease. Appendix D. Quality Assessment Forms. Rockville: Agency for Healthcare Research and Quality (US), 2004.
21. National Institute for Health and Care Excellence. Appendix 4. Quality assessment for Case series. 2013. Available online: https://www.nice.org.uk/guidance/cg3/documents/appendix-4-quality-of-case-series-form2
22. DerSimonian R, Kacker R. Random-effects model for meta-analysis of clinical trials: an update. Contemp Clin Trials 2007;28:105-14.
23. Guyatt G, Oxman AD, Akl EA, et al. GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. J Clin Epidemiol 2011;64:383-94.
24. Norris SL, Meerpohl JJ, Akl EA, et al. The skills and experience of GRADE methodologists can be assessed with a simple tool. J Clin Epidemiol 2016;79:150-8.e1.
25. Guyatt GH, Oxman AD, Vist G, et al. GRADE guidelines: 4. Rating the quality of evidence--study limitations (risk of bias). J Clin Epidemiol 2011;64:407-15.
26. Guyatt GH, Oxman AD, Montori V, et al. GRADE guidelines: 5. Rating the quality of evidence--publication bias. J Clin Epidemiol 2011;64:1277-82.
27. Guyatt GH, Oxman AD, Kunz R, et al. GRADE guidelines 6. Rating the quality of evidence--imprecision. J Clin Epidemiol 2011;64:1283-93.
28. Guyatt GH, Oxman AD, Kunz R, et al. GRADE guidelines: 7. Rating the quality of evidence--inconsistency. J Clin Epidemiol 2011;64:1294-302.

29. Guyatt GH, Oxman AD, Kunz R, et al. GRADE guidelines: 8. Rating the quality of evidence--indirectness. J Clin Epidemiol 2011;64:1303-10.
30. Guyatt GH, Oxman AD, Sultan S, et al. GRADE guidelines: 9. Rating up the quality of evidence. J Clin Epidemiol 2011;64:1311-6.
31. Ge L, Tian JH, Li YN, et al. Association between prospective registration and overall reporting and methodological quality of systematic reviews: a meta-epidemiological study. J Clin Epidemiol 2018;93:45-55.
32. Deng H, Zhang Y, Wang Y, et al. Two cases of novel coronavirus infection in children. Pediatr Emerg Med 2020;27:81-3.
33. Cai JH, Wang XS, Ge YL, et al. First case of 2019 novel coronavirus infection in children in Shanghai. Zhonghua Er Ke Za Zhi 2020;58:86-7.
34. Zhang YH, Lin DJ, Xiao MF, et al. 2019-novel coronavirus infection in a three-month-old baby. Zhonghua Er Ke Za Zhi 2020;58:182-4.
35. Wei M, Yuan J, Liu Y, et al. Novel Coronavirus Infection in Hospitalized Infants Under 1 Year of Age in China. JAMA 2020;323:1313-4.
36. Chen F, Liu ZS, Zhang FR, et al. First case of severe childhood novel coronavirus pneumonia in China. Zhonghua Er Ke Za Zhi 2020;58:179-82.
37. Zeng LK, Tao XW, Yuan WH, et al. First case of neonate infected with novel coronavirus pneumonia in China. Zhonghua Er Ke Za Zhi 2020;58:E009.
38. Feng K, Yun YX, Wang XF, et al. Analysis of CT features of 15 Children with 2019 novel coronavirus infection. Zhonghua Er Ke Za Zhi 2020;58:275-8.
39. Wang H, Duan X, Yan X, et al. A case of novel coronavirus pneumonia complicated with acute appendicitis in children. Chin J Pediatr Surg 2020. doi: 10.1101/2020.04.13.20064352.
40. Quan S, Li X, Ding D, et al. A case of novel coronavirus infection in children in Liaoning. Pediatr Emerg Med 2020. doi: 10.3760/cma.j.issn.1673-4912.2020.0005.
41. Xiong D, Jiang J, Feng Y, et al. Novel coronavirus pneumonia in children: a report of two cases. Pediatr Emerg Med 2020. doi: 10.3760/cma.j.issn.1673-4912.2020.0002.
42. Cai J, Xu J, Lin D, et al. A case series of children with 2019 novel coronavirus infection: clinical and epidemiological features. Clin Infect Dis 2020;58:E269.
43. Wang D, Ju XL, Xie F, 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 2020;58:E011.
44. Tang A, Xu W, Shen M, et al. A retrospective study of the clinical characteristics of COVID-19 infection in 26 children. medRxiv 2020. doi: 10.1101/2020.03.08.20029710.
45. Liu W, Zhang Q, Chen J, et al. Detection of Covid-19 in Children in Early January 2020 in Wuhan, China. N Engl J Med 2020;382:1370-1.
46. Lu X, Zhang L, Du H, et al. SARS-CoV-2 Infection in Children. N Engl J Med 2020;382:1663-5.
47. Ma H, Hu J, Tian J, et al. Visualizing the novel coronavirus (COVID-19) in children: What we learn from patients at Wuhan Children's Hospital. SSRN 2020. Available online: https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3556676
48. Zhao R, Shen X, Xu K, et al. A case of 2019 novel coronavirus infection in children. Zhejiang Medical Journal 2020;42:305-6.
49. Li Q, Peng X, Sun Z, et al. Clinical and imaging characteristics of children with corona virus disease 2019 (COVID-19). Radiol Practice 2020;35:277-80.
50. Zhang X, Ma Y, Xiao J, et al. Clinical characteristics of novel coronavirus pneumonia in children in Jinan. Journal of Shandong University (Health Sciences) 2020;58:62-4.
51. Zhang GX, Zhang AM, Huang L, et al. Twin girls infected with SARS-CoV-2. Zhongguo Dang Dai Er Ke Za Zhi 2020;22:221-5.
52. Liu M, Wan X, Tu X, et al. Family cluster of child SARS-CoV-2 infections: a case report. Medical Journal of Wuhan University 2020;3:362-5.
53. Xiao K, Shui L, Pang X, et al. The clinical features of the 143 patients with COVID-19 in North-East of Chongqing. Journal of Third Military Medical University 2020. doi: 10.16016/j.1000-5404.202002097.
54. Xu H, Liu E, Xie J, et al. A follow-up study of children infected with SARS-CoV-2 from Western China. medRXiv 2020. doi: 10.1101/2020.04.20.20073288.
55. 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.
56. Kam KQ, Yung CF, Cui L, et al. A Well Infant with Coronavirus Disease 2019 (COVID-19) with High Viral Load. Clin Infect Dis 2020. [Epub ahead of print].
57. Park JY, Han MS, Park KU, et al. First Pediatric Case of Coronavirus Disease 2019 in Korea. J Korean Med Sci 2020;35:e124.
58. Du W, Yu J, Wang H, et al. Clinical characteristics of

COVID-19 in children compared with adults outside of Hubei Province in China. SSRN 2020. doi: 10.2139/ssrn.3546097.
59. Liu H, Liu F, Li J, et al. Clinical and CT imaging features of the COVID-19 pneumonia: Focus on pregnant women and children. J Infect J Infect 2020;80:e7-13.
60. Wang S, Guo L, Chen L, et al. A case report of neonatal COVID-19 infection in China. Clin Infect Dis 2020. [Epub ahead of print].
61. Rahimzadeh G, Ekrami NM, Kadkhodaei EF, et al. COVID-19 Infection in Iranian Children: A Case Series of 9 Patients. Journal of Pediatrics Review 2020;8:139-44.
62. Ji LN, Chao S, Wang Y, et al. Clinical features of pediatric patients with COVID-19: a report of two family cluster cases. World J Pediatr 2020. [Epub ahead of print].
63. Xu Y, Li X, Zhu B, et al. Characteristics of pediatric SARS-CoV-2 infection and potential evidence for persistent fecal viral shedding. Nat Med 2020;26:502-5.
64. Xia W, Shao J, Guo Y, et al. Clinical and CT features in pediatric patients with COVID-19 infection: Different points from adults. Pediatr Pulmonol 2020;55:1169-74.
65. Dong Y, Mo X, Hu Y, et al. Epidemiological characteristics of 2143 pediatric patients with 2019 coronavirus disease in China. Pediatrics 2020. doi: 10.1542/peds.2020-0702.
66. Xing Y, Ni W, Wu Q, et al. Prolonged presence of SARS-CoV-2 in feces of pediatric patients during the convalescent phase. medRxiv 2020. doi: 10.1101/2020.03.11.20033159.
67. Yu H, Cai Q, Dai X, et al. The clinical and epidemiological features and hints of 82 confirmed COVID-19 pediatric cases aged 0-16 in Wuhan, China. medRxiv 2020. doi: 10.1101/2020.03.15.20036319.
68. Liu J, Luo W, Deng Z, et al. Clinical and epidemiological characteristics of 91 children conformed with COVID-19. Chin J Nosocomiol 2020;30:1645-9.
69. Ma YL, Xia SY, Wang M, et al. Clinical features of children with SARS-CoV-2 infection: an analysis of 115 cases. Zhongguo Dang Dai Er Ke Za Zhi 2020;22:290-3.
70. Qian G, Yang N, Ma AHY, et al. A COVID-19 Transmission within a family cluster by presymptomatic infectors in China. Clin Infect Dis 2020. [Epub ahead of print].
71. Qiu H, Wu J, Hong L, et al. Clinical and epidemiological features of 36 children with coronavirus disease 2019 (COVID-19) in Zhejiang, China: an observational cohort study. Lancet Infect Dis 2020. [Epub ahead of print].
72. Zheng F, Liao C, Fan Q, et al. Clinical characteristics of children with coronavirus disease 2019 in Hubei, China. Curr Med Sci 2020;40:275-80.
73. Sun D, Li H, Lu X, et al. Clinical features of severe pediatric patients with coronavirus disease 2019 in Wuhan: a single center's observational study. World J Pediatr 2020. [Epub ahead of print].
74. Dong X, Cao Y, Lu X, et al. Eleven faces of coronavirus disease 2019. Allergy 2020. [Epub ahead of print].
75. Wu Q, Xing Y, Shi L, et al. Epidemiological and clinical characteristics of children with coronavirus disease 2019. medRxiv 2020. doi: 10.1101/2020.03.19.20027078.
76. 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.
77. Le HT, Nguyen LV, Tran DM, et al. The first infant case of COVID-19 acquired from a secondary transmission in Vietnam. Lancet Child Adolesc Health 2020;4:405-6.
78. Zhong Z, Xie X, Huang W, et al. Chest CT findings and clinical features of coronavirus disease 2019 in children. Zhong Nan Da Xue Xue Bao Yi Xue Ban 2020;45:236-42.
79. Yang L, Li Z, Xu H, et al. Epidemiological and clinical characteristics of 10 children with coronavirus disease (COVID-19) in Jinan City. Journal of Shandong University (Health Sciences) 2020;58:36-9.
80. Tang A, Tong ZD, Wang HL, et al. Detection of Novel Coronavirus by RT-PCR in Stool Specimen from Asymptomatic Child, China. Emerg Infect Dis 2020. [Epub ahead of print].
81. Epidemiology Working Group for NCIP Epidemic Response, Chinese Center for Disease Control and Prevention. The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China. Zhonghua Liu Xing Bing Xue Za Zhi 2020;41:145-51.
82. Zhang J, Dong X, Cao Y, et al. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. Allergy 2020. [Epub ahead of print].
83. Li YY, Wang WN, Lei Y, et al. Comparison of the clinical characteristics between RNA positive and negative patients clinically diagnosed with 2019 novel coronavirus pneumonia. Zhonghua Jie He He Hu Xi Za Zhi 2020;43:E023.
84. Chen L, Liu HG, Liu W, et al. Analysis of clinical features of 29 patients with 2019 novel coronavirus pneumonia. Zhonghua Jie He He Hu Xi Za Zhi 2020;43:203-8.
85. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020;395:497-506.

86. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020;395:507-13.
87. Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA 2020. [Epub ahead of print].
88. Hu Z, Song C, Xu C, et al. Clinical characteristics of 24 asymptomatic infections with COVID-19 screened among close contacts in Nanjing, China. Sci China Life Sci 2020;63:706-11.
89. Pediatric Branch of Hubei Medical Association, Pediatric Branch of Wuhan Medical Association, Pediatric Medical Quality Control Center of Hubei. Recommendation for the diagnosis and treatment of novel coronavirus infection in children in Hubei (Trial version 1). Zhongguo Dang Dai Er Ke Za Zhi 2020;22:96-9.
90. Chen Z, Fu J, Shu Q, et al. Diagnosis and treatment recommendation for pediatric COVID-19 (the second edition). Zhejiang Da Xue Xue Bao Yi Xue Ban 2020;49:139-46.
91. Xu H, Luo Zh, Xu F. Diagnosis and treatment of the 2019 novel coronavirus infection in children. (Trial version 2 of Children's Hospital of Chongqing Medical University). Journal of Pediatric Pharmacy 2020. Available online: http://kns.cnki.net/kcms/detail/50.1156.R.20200226.1309.002.html
92. Wang M, Yue S. The programme for prevention and control of SARS-CoV-2 infection in neonates in Hunan Provence. China J Mod Med 2020:65-71.
93. Li ZZ, Shen KL, Wei XM, et al. Clinical analysis of pediatric SARS cases in Beijing. Zhonghua Er Ke Za Zhi 2003;41:574-7.
94. Memish ZA, Al-Tawfiq JA, Assiri A, et al. Middle East respiratory syndrome coronavirus disease in children. Pediatr Infect Dis J 2014;33:904-6.
95. Young BE, Ong SWX, Kalimuddin S, et al. Epidemiologic features and clinical course of patients infected with SARS-CoV-2 in Singapore. JAMA 2020. [Epub ahead of print].
96. Ong SWX, Tan YK, Chia PY, et al. Air, surface environmental, and personal protective equipment contamination by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from a symptomatic patient. JAMA 2020. [Epub ahead of print].
97. Rodriguez-Morales AJ, Cardona-Ospina JA, Gutiérrez-Ocampo E, et al. Clinical, laboratory and imaging features of COVID-19: A systematic review and meta-analysis. Travel Med Infect Dis 2020. [Epub ahead of print].
98. Pei Y, Liu W, Ismail BM, et al. COVID-19: Children comparison with adults based on the latest data. SSRN 2020. doi: 10.2139/ssrn.3550063.
99. Li LQ, Huang T, Wang YQ, et al. COVID-19 patients' clinical characteristics, discharge rate, and fatality rate of meta-analysis. J Med Virol 2020. [Epub ahead of print].
100. Qian K, Deng Y, Tai Y, et al. Clinical characteristics of 2019 novel infected coronavirus pneumonia: a systemic review and meta-analysis. medrxiv 2020.doi: 10.1101/2020.02.14.20021535
101. Sun P, Qie S, Liu Z, et al. Clinical characteristics of hospitalized patients with SARS-CoV-2 infection: a single arm meta-analysis. J Med Virol 2020. [Epub ahead of print].
102. Fang Z, Yi F, Wu K, et al. Clinical characteristics of coronavirus disease 2019 (COVID-19): an updated systematic review. medrxiv 2020. doi: 10.1101/2020.03.07.20032573.
103. Ludvigsson JF. Systematic review of COVID-19 in children shows milder cases and a better prognosis than adults. Acta Paediatr 2020;109:1088-95.
104. World Health Organization. WHO handbook for guideline development, 2nd ed. 2014. Available online: https://apps.who.int/iris/handle/10665/145714

Cite this article as: Wang Z, Zhou Q, Wang C, Shi Q, Lu S, Ma Y, Luo X, Xun Y, Li W, Baskota M, Yang Y, Zhai H, Fukuoka T, Ahn HS, Lee MS, Luo Z, Liu E, Chen Y; on behalf of COVID-19 Evidence and Recommendations Working Group. Clinical characteristics of children with COVID-19: a rapid review and meta-analysis. Ann Transl Med 2020;8(10):620. doi: 10.21037/atm-20-3302

Supplementary

Supplementary File I Search strategy

PubMed

#1 "Epidemiological Studies"[Title/Abstract]
#2 "Epidemiologic* Study"[Title/Abstract]
#3 "Epidemiological characteristics"[Title/Abstract]
#4 "Clinical features"[Title/Abstract]
#5 "Clinical characteristics"[Title/Abstract]
#6 "Clinical Presentation"[Title/Abstract]
#7 #1-#6/ OR
#8 "COVID-19"[Supplementary Concept]
#9 "Severe Acute Respiratory Syndrome Coronavirus 2"[Supplementary Concept]
#10 "COVID-19"[Title/Abstract]
#11 "SARS-COV-2"[Title/Abstract]
#12 "Novel coronavirus" [Title/Abstract]
#13 "2019-novel coronavirus" [Title/Abstract]
#14 "coronavirus disease-19" [Title/Abstract]
#15 "coronavirus disease 2019" [Title/Abstract]
#16 "COVID19" [Title/Abstract]
#17 "Novel CoV" [Title/Abstract]
#18 "2019-nCoV" [Title/Abstract]
#19 "2019-CoV" [Title/Abstract]
#20 #8-#19/ OR
#21 #7 AND #20

EMBASE

#1 'COVID-19':ab,ti
#2 'SARS-COV-2':ab,ti
#3 'novel coronavirus':ab,ti
#4 '2019-novel coronavirus':ab,ti
#5 'coronavirus disease-19':ab,ti
#6 'coronavirus disease 2019':ab,ti
#7 'COVID19':ab,ti
#8 'novel cov':ab,ti
#9 '2019-ncov':ab,ti
#10 '2019-cov':ab,ti
#11 #1-10/OR
#12 'epidemiological studies':ab,ti
#13 'epidemiologic* study':ab,ti
#14 'epidemiological characteristics':ab,ti
#15 'clinical feature'/exp
#16 'clinical features':ab,ti
#17 'clinical characteristics':ab,ti
#18 'clinical presentation':ab,ti
#19 #12-18/OR
#20 #11 AND #19
#21 #20 AND [medline]/lim
#22 #20 NOT #21

Web of Science

#1 TOPIC: "Epidemiological Studies"
#2 TOPIC: "Epidemiologic* Study"
#3 TOPIC: "Epidemiological characteristics"
#4 TOPIC: "Clinical features"
#5 TOPIC: "Clinical characteristics"
#6 TOPIC: "Clinical Presentation"
#7 #1-6/OR
#8 TOPIC: "COVID-19"
#9 TOPIC: "SARS-COV-2"
#10 TOPIC: "Novel coronavirus"
#11 TOPIC: "2019-novel coronavirus"
#12 TOPIC: "coronavirus disease-19"
#13 TOPIC: "coronavirus disease 2019"
#14 TOPIC: "COVID19"
#15 TOPIC: "Novel CoV"
#16 TOPIC: "2019-nCoV"
#17 TOPIC: "2019-CoV"
#18 #8-17/ OR
#19 #7 AND #18

Cochrane

#1 "COVID-19":ti,ab,kw
#2 "SARS-COV-2":ti,ab,kw
#3 "Novel coronavirus":ti,ab,kw
#4 "2019-novel coronavirus" :ti,ab,kw
#5 "Novel CoV" :ti,ab,kw
#6 "2019-nCoV" :ti,ab,kw
#7 "coronavirus disease-19" :ti,ab,kw
#8 "coronavirus disease 2019" :ti,ab,kw
#9 "COVID19" :ti,ab,kw
#10 #1-9/OR
#11 "Epidemiological Studies":ti,ab,kw
#12 "Epidemiologic* Study":ti,ab,kw
#13 "Epidemiological characteristics":ti,ab,kw
#14 "Clinical features":ti,ab,kw
#15 "Clinical characteristics":ti,ab,kw
#16 "Clinical Presentation":ti,ab,kw
#17 #11-16/ OR
#18 #10 AND #17

CBM

#1 "新型冠状病毒"[常用字段:智能]
#2 "COVID-19"[常用字段:智能]
#3 "COVID 19"[常用字段:智能]
#4 "2019-nCoV"[常用字段:智能]
#5 "2019-CoV"[常用字段:智能]
#6 "SARS-CoV-2"[常用字段:智能]
#7 #1-6/OR
#8 "流行病学"[中文标题:智能]
#9 "临床表现"[中文标题:智能]
#10 "临床特征"[中文标题:智能]
#11 "临床特点"[中文标题:智能]
#12 #8-11/ OR
#13 #7 AND #12

WanFang

#1 "新型冠状病毒"[主题]
#2 "COVID-19"[主题]
#3 "COVID 19"[主题]
#4 "2019-nCoV"[主题]
#5 "2019-CoV"[主题]
#6 "SARS-CoV-2"[主题]
#7 #1-#6/ OR
#8 "流行病学"[题名]
#9 "临床特点"[题名]
#10 "临床特征"[题名]
#11 "临床表现"[题名]
#12 #8-11/ OR
#13 #7 AND #12

CNKI

#1 "新型冠状病毒"[主题]
#2 "COVID-19"[主题]
#3 "COVID 19"[主题]
#4 "2019-nCoV"[主题]
#5 "2019-CoV"[主题]
#6 "SARS-CoV-2"[主题]
#7 #1-6/ OR
#8 "流行病学"[篇名]
#9 "临床特点"[篇名]
#10 "临床特征"[篇名]
#11 "临床表现"[篇名]
#12 #8-11 OR
#13 #7 AND #12

Supplementary File II Risk of bias

Table A National Institute for Health and Care Excellence

Author	1. Case series collected in more than one centre, i.e., multi-centre study	2. Is the hypothesis/aim/ objective of the study clearly described?	3. Are the inclusion and exclusion criteria (case definition) clearly reported?	4. Is there a clear definition of the outcomes reported?	5. Were data collected prospectively?	6. Is there an explicit statement that patients were recruited consecutively?	7. Are the main findings of the study clearly described?	8. Are outcomes stratified? (e.g., by disease stage, abnormal test results, patient characteristics)	Total Score
Deng 2020, (32)	No	Yes	Yes	No	Yes	No	Yes	No	4
Cai 2020, (33)	No	Yes	Yes	No	Yes	No	Yes	No	4
Zhang 2020, (34)	No	Yes	Yes	No	Yes	No	Yes	No	4
Wei 2020, (35)	Yes	Yes	Yes	Yes	No	No	Yes	No	5
Chen 2020, (36)	No	Yes	Yes	Yes	Yes	No	Yes	No	5
Zeng 2020, (37)	No	Yes	Yes	Yes	Yes	No	Yes	No	5
Feng 2020, (38)	No	Yes	Yes	Yes	No	No	Yes	Yes	5
Wang 2020, (39)	No	Yes	Yes	No	Yes	No	Yes	No	4
Quan 2020, (40)	No	Yes	Yes	No	Yes	No	Yes	No	4
Xiong 2020, (41)	No	Yes	Yes	No	Yes	No	Yes	No	4
Cai 2020, (42)	Yes	Yes	Yes	No	Yes	No	Yes	No	5
Wang 2020, (43)	Yes	Yes	Yes	Yes	No	No	Yes	No	5
Tang 2020, (44)	No	Yes	Yes	Yes	No	No	Yes	No	4
Liu 2020, (45)	Yes	Yes	Yes	Yes	No	No	Yes	Yes	6
Lu 2020, (46)	No	Yes	Yes	No	Yes	No	Yes	Yes	5
Ma 2020, (47)	No	Yes	No	No	No	No	Yes	Yes	3
Zhao 2020, (48)	No	Yes	No	Yes	No	No	Yes	Yes	4
Li 2020, (49)	Yes	Yes	Yes	Yes	No	No	Yes	No	5
Zhang 2020, (50)	No	Yes	Yes	Yes	No	No	Yes	No	4
Zhang 2020, (51)	No	Yes	No	No	No	No	Yes	Yes	3
Liu 2020, (52)	No	Yes	No	No	No	No	Yes	Yes	3
Xiao 2020, (53)	No	Yes	Yes	Yes	No	No	Yes	Yes	5
Xu 2020, (54)	Yes	Yes	Yes	Yes	No	No	Yes	Yes	5
Chan 2020, (55)	No	Yes	Yes	Yes	No	Yes	Yes	Yes	6
Kam 2020, (56)	No	Yes	No	Yes	No	No	Yes	Yes	4
Park 2020, (57)	No	Yes	No	No	No	No	Yes	Yes	3
Du 2020, (58)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	7
Liu 2020, (59)	Yes	Yes	No	Yes	No	No	Yes	Yes	5
Wang 2020, (60)	No	Yes	No	Yes	No	No	Yes	Yes	4
Rahimzadeh 2020, (61)	Yes	Yes	No	No	No	No	Yes	Yes	4
Ji 2020, (62)	No	Yes	No	Yes	No	No	Yes	Yes	4
Xu 2020, (63)	No	Yes	Yes	No	No	No	Yes	Yes	4
Xia 2020, (64)	No	Yes	Yes	Yes	No	No	Yes	No	4
Dong 2020, (65)	Yes	Yes	Yes	Yes	No	No	Yes	Yes	6
Xing 2020, (66)	No	Yes	Yes	Yes	No	No	Yes	Yes	5
Yu 2020, (67)	No	Yes	Yes	No	No	No	Yes	Yes	4
Liu 2020, (68)	No	Yes	Yes	Yes	No	No	Yes	Yes	5
MA 2020, (69)	No	Yes	Yes	Yes	No	No	Yes	Yes	5
Qian 2020, (70)	No	Yes	No	No	No	No	Yes	Yes	3
Zhang 2020, (72)	Yes	Yes	Yes	Yes	No	No	Yes	Yes	6
Sun 2020, (73)	No	Yes	Yes	Yes	No	No	Yes	No	4
Dong 2020, (74)	Yes	Yes	No	Yes	No	No	Yes	Yes	5
Wu 2020, (75)	Yes	Yes	Yes	Yes	No	No	Yes	No	5
Su 2020, (76)	No	Yes	Yes	Yes	No	No	Yes	Yes	5
Le 2020, (77)	No	Yes	No	No	No	No	Yes	Yes	3
Zhong 2020, (78)	No	Yes	Yes	Yes	No	No	Yes	Yes	5
Liu 2020, (79)	Yes	Yes	Yes	Yes	No	No	Yes	Yes	6
Tang 2020, (80)	No	Yes	No	No	No	No	Yes	Yes	3

Table B Newcastle-Ottawa Scale

Author	SELECTION				COMPARABILITY	OUTCOME		
	1) Representativeness of the Exposed Cohort	2) Selection of the Non-Exposed Cohort	3) Ascertainment of Exposure	4) Demonstration That Outcome of Interest Was Not Present at Start of Study	1) Comparability of Cohorts on the Basis of the Design or Analysis	1) Assessment of Outcome	2) Was Follow-Up Long Enough for Outcomes to Occur	3) Adequacy of Follow Up of Cohorts
Qiu 2020, (71)	☆		☆	☆		☆		

☆ means one star, which have been explained in the part of the “Risk of bias assessment”.

Supplementary File III GRADE evidence profile

Table C Symptoms and imaging findings

No. of studies	Certainty assessment					No. of patients		Effect value (95% CI)	Certainty
	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Total	Event		
The overall symptoms									
No symptom, (17)	Serious[1]	Serious[2]	Not serious	Not serious	None	1,396	218	19% (14%, 23%)	⨁⨁◯◯ Low
Mild symptom, (19)	Serious[1]	Serious[2]	Not serious	Not serious	None	1,540	1,396	94% (90%, 98%)	⨁⨁◯◯ Low
Severe symptom, (19)	Serious[1]	Not serious	Not serious	Not serious	None	1,525	49	3% (2%, 4%)	⨁⨁⨁◯ Moderate
More than one sign or symptom, (15)	Serious[1]	Serious[2]	Not serious	Not serious	None	281	104	35% (21%, 48%)	⨁⨁◯◯ Low
Specific symptoms									
Fever, (22)	Serious[1]	Serious[2]	Not serious	Not serious	None	890	418	48% (39%, 56%)	⨁⨁◯◯ Low
Cough, (20)	Serious[1]	Serious[2]	Not serious	Not serious	None	766	352	39% (30%, 48%)	⨁⨁◯◯ Low
Fever and cough, (7)	Serious[1]	Serious[2]	Not serious	Not serious	None	203	76	30% (18%, 42%)	⨁⨁◯◯ Low
Sputum production, (4)	Serious[1]	Serious[2]	Not serious	Serious[3]	None	292	92	19% (0%, 44%)	⨁◯◯◯ Very low
Rhinorrhoea, (9)	Serious[1]	Not serious	Not serious	Not serious	None	380	37	9% (6%, 12%)	⨁⨁⨁◯ Moderate
Shortness of breath/dyspnoea, (6)	Serious[1]	Serious[2]	Not serious	Not serious	None	343	64	9% (0%, 19%)	⨁⨁◯◯ Low
Myalgia or fatigue, (10)	Serious[1]	Serious[2]	Not serious	Not serious	None	524	49	8% (5%, 12%)	⨁⨁◯◯ Low
Diarrhoea, (10)	Serious[1]	Not serious	Not serious	Not serious	None	528	42	7% (5%, 9%)	⨁⨁⨁◯ Moderate
Nausea or vomiting, (8)	Serious[1]	Not serious	Not serious	Not serious	None	430	27	6% (4%, 9%)	⨁⨁⨁◯ Moderate
Nasal obstruction, (6)	Serious[1]	Not serious	Not serious	Not serious	None	262	19	6% (3%, 9%)	⨁⨁⨁◯ Moderate
Sore throat, (10)	Serious[1]	Not serious	Not serious	Not serious	None	244	20	6% (2%, 10%)	⨁⨁⨁◯ Moderate
Headache, (7)	Serious[1]	Not serious	Not serious	Not serious	None	289	14	4% (1%, 6%)	⨁⨁⨁◯ Moderate
Imaging findings									
Abnormal, (18)	Serious[1]	Serious[2]	Not serious	Not serious	None	674	447	66% (55%, 77%)	⨁⨁◯◯ Low
Unilateral pneumonia, (10)	Serious[1]	Serious[2]	Not serious	Not serious	None	347	111	31% (20%, 43%)	⨁⨁◯◯ Low
Bilateral pneumonia, (13)	Serious[1]	Serious[2]	Not serious	Not serious	None	597	146	28% (20%, 36%)	⨁⨁◯◯ Low
Ground-glass opacity, (14)	Serious[1]	Serious[2]	Not serious	Not serious	None	727	246	35% (26%, 44%)	⨁⨁◯◯ Low

Table D Laboratory results

No. of studies	Certainty assessment					No. of patients	Effect value (95% CI)	Certainty
	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Total		
Blood routine values								
Leucocytes (×10^9/L), (11)	Serious[1]	Not serious	Not serious	Not serious	None	465	6.60 (6.19, 7.01)	⨁⨁⨁◯◯ Moderate
Lymphocytes (×10^9/L), (8)	Serious[1]	Serious[2]	Not serious	Not serious	None	356	2.76 (2.47, 3.05)	⨁⨁◯◯ Low
Neutrophils (×10^9/L), (5)	Serious[1]	Serious[2]	Not serious	Not serious	None	236	2.70 (2.10, 3.31)	⨁⨁◯◯ Low
Platelets (×10^9/L), (6)	Serious[1]	Serious[2]	Not serious	Not serious	None	133	257.09 (251.06, 263.13)	⨁⨁◯◯ Low
Haemoglobin (g/L), (7)	Serious[1]	Serious[2]	Not serious	Not serious	None	304	127.61 (123.80, 131.41)	⨁⨁◯◯ Low
Blood biochemistry								
Albumin (g/L), (2)	Serious[1]	Not serious	Not serious	Not serious	None	41	45.30 (45.13, 45.47)	⨁⨁⨁◯ Moderate
Alanine aminotransferase (U/L), (8)	Serious[1]	Serious[2]	Not serious	Serious[3]	None	306	20.46 (14.51, 26.41)	⨁◯◯◯ Very low
Aspartate aminotransferase (U/L), (7)	Serious[1]	Serious[2]	Not serious	Not serious	None	281	32.04 (30.25, 33.83)	⨁⨁◯◯ Low
Total bilirubin (μmol/L), (2)	Serious[1]	Serious[2]	Not serious	Serious[3]	None	41	8.14 (1.45, 14.82)	⨁◯◯◯ Very low
Blood urea nitrogen (mmol/L), (5)	Serious[1]	Not serious	Not serious	Not serious	None	240	3.81 (3.43, 4.18)	⨁⨁⨁◯ Moderate
Creatinine (μmol/L), (5)	Serious[1]	Serious[2]	Not serious	Serious[3]	None	240	41.60 (32.98, 50.22)	⨁◯◯◯ Very low
Creatine kinase (U/L), (3)	Serious[1]	Serious[2]	Not serious	Not serious	None	59	104.37 (95.66, 113.08)	⨁⨁◯◯ Low
Lactate dehydrogenase (U/L), (7)	Serious[1]	Serious[2]	Not serious	Serious[3]	None	334	264.43 (241.85, 287.02)	⨁◯◯◯ Very low
Myoglobin (ug/L), (2)	Serious[1]	Not serious	Not serious	Not serious	None	23	15.33 (11.18, 19.48)	⨁⨁⨁◯ Moderate
Procalcitonin (g/L), (7)	Serious[1]	Not serious	Not serious	Not serious	None	398	0.06 (0.00, 0.16)	⨁⨁⨁◯ Moderate
CRP (mg/L), (8)	Serious[1]	Serious[2]	Not serious	Not serious	None	348	5.05 (1.86, 8.24)	⨁⨁◯□ Low
Coagulation function								
Activated partial thromboplastin time(s), (2)	Serious[1]	Serious[2]	Not serious	Serious[3]	None	38	37.59 (28.69, 46.48)	⨁◯◯◯ Very low
Prothrombin time(s), (4)	Serious[1]	Serious[2]	Not serious	Not serious	None	223	12.25 (11.30, 13.20)	⨁⨁◯◯ Low
D-dimer (mg/L), (8)	Serious[1]	Not serious	Not serious	Not serious	None	261	0.33 (0.17, 0.49)	⨁⨁⨁◯ Moderate

Explanations
1. downgrade one level: The risk of bias is high due to the limitations of study design.
2. downgrade one level: Heterogeneity of data synthesis results, I^2>50%.
3. downgrade one level: Sample size is less than optimal information sample (OIS).
4. upgrade two levels: Large magnitude of effect, RR >5.
5. Outcome (number of studies)

Supplementary File IV Case report summary

Table E Symptom

Study ID	Number	Mild symptom	Severe symptom	Fever	Cough	Fever and cough	Sputum production	Myalgia or fatigue	Sore throat	Shortness of breath/dyspnoea	Diarrhoea	Headache	Nasal obstruction	Rhinorrhoea	Nausea or vomiting	No symptom	More than one sign or symptom
Deng 2020, (32)	2	2/2	0/2	1/2	0/2	0/2	0/2	0/2	1/2	0/2	0/2	0/2	0/2	0/2	0/2	0/2	0/2
Cai 2020, (33)	1	1/1	0/1	1/1	1/1	1/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	1/1	0/1	1/1
Zhang 2020, (34)	1	1/1	0/1	1/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1
Chen 2020, (36)	1	0/1	1/1	1/1	0/1	0/1	0/1	0/1	0/1	0/1	1/1	0/1	0/1	0/1	1/1	0/1	1/1
Zeng 2020, (37)	1	1/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	1/1
Wang 2020, (39)	1	1/1	0/1	1/1	1/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	1/1	0/1	1/1
Quan 2020, (40)	1	1/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	1/1	0/1
Xiong 2020, (41)	2	2/2	0/2	2/2	2/2	2/2	0/2	0/2	0/2	0/2	1/2	0/2	0/2	1/2	0/2	0/2	2/2
Liu 2020, (45)	6	5/6	1/6	6/6	6/6	6/6	0/6	0/6	0/6	1/6	0/6	0/6	0/6	1/6	4/6	0/6	6/6
Zhao 2020, (48)	1	1/1	0/1	1/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1
Zhang 2020, (51)	2	2/2	0/2	2/2	2/2	2/2	0/2	0/2	0/2	0/2	1/2	0/2	0/2	0/2	0/2	0/2	2/2
Liu 2020, (52)	1	1/1	0/1	1/1	0/1	0/1	0/1	0/1	0/1	0/1	1/1	0/1	0/1	0/1	1/1	0/1	1/1
Xiao 2020, (53)	1	1/1	0/1	1/1	1/1	1/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	1/1	0/1	0/1	1/1
Chan 2020, (55)	1	1/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	1/1	0/1
Kam 2020, (56)	1	1/1	0/1	1/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1
Park 2020, (57)	1	1/1	0/1	1/1	0/1	0/1	1/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	1/1
Liu 2020, (59)	4	4/4	0/4	3/4	3/4	2/4	0/4	1/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	2/4
Wang 2020, (60)	1	1/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	1/1	0/1
Ji 2020, (62)	2	2/2	0/2	1/2	0/2	0/2	0/2	0/2	0/2	0/2	1/2	0/2	0/2	0/2	0/2	0/2	0/2
Xing 2020, (66)	3	3/3	0/3	3/3	0/3	0/3	0/3	0/3	0/3	0/3	0/3	0/3	0/3	0/3	0/3	0/3	0/3
Qian, (70)	1	1/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	1/1	0/1
Sun, (73)	8	0/8	8/8	6/8	6/8	4/8	4/8	1/8	0/8	8/8	3/8	1/8	0/8	0/8	4/8	0/8	8/8
Dong, (74)	2	2/2	0/2	1/2	1/2	1/2	1/2	0/2	0/2	0/2	0/2	0/2	0/2	0/2	0/2	0/2	1/2
Le, (77)	1	1/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	1/1	1/1	0/1	0/1	1/1
Tang, (80)	1	1/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	1/1	0/1

Table F Imaging findings and family contact

Study ID	Number	Abnormal	Unilateral pneumonia	Bilateral pneumonia	Ground-glass opacity	Family contact
Deng 2020, (32)	2	0/2	0/2	0/2	0/2	2/2
Cai 2020, (33)	1	1/1	NR/1	NR/1	NR/1	1/1
Zhang 2020, (34)	1	1/1	NR/1	NR/1	NR/1	NR/1
Chen 2020, (36)	1	1/1	1/1	0/1	1/1	0/1
Zeng 2020, (37)	1	1/1	0/1	1/1	0/1	1/1
Wang 2020, (39)	1	1/1	1/1	0/1	1/1	1/1
Quan 2020, (40)	1	1/1	1/1	0/1	0/1	1/1
Xiong 2020, (41)	2	2/2	2/2	0/2	1/2	2/2
Liu 2020, (45)	6	4/5	0/5	4/5	1/5	0/6
Zhao 2020, (48)	1	1/1	1/1	0/1	0/1	1/1
Zhang 2020, (51)	2	1/2	0/2	1/2	NR/2	2/2
Liu 2020, (52)	1	1/1	0/1	1/1	1/1	1/1
Xiao 2020, (53)	1	1/1	0/1	1/1	0/1	1/1
Chan 2020, (55)	1	1/1	NR/1	NR/1	1/1	1/1
Kam 2020, (56)	1	NR/1	NR/1	NR/1	NR/1	1/1
Park 2020, (57)	1	1/1	1/1	0/1	1/1	1/1
Liu 2020, (59)	4	3/4	NR/4	NR/4	1/4	NR/4
Wang 2020, (60)	1	1/1	NR/1	NR/1	NR/1	1/1
Ji 2020, (62)	2	0/2	0/2	0/2	0/2	2/2
Xing 2020, (66)	3	2/3	2/3	0/3	2/3	3/3
Qian, (70)	1	NR/1	NR/1	NR/1	NR/1	1/1
Sun, (73)	8	8/8	2/8	6/8	6/8	5/8
Dong, (74)	2	1/2	0/2	1/2	NR/2	NR/2
Le, (77)	1	0/1	0/1	0/1	0/1	1/1
Tang, (80)	1	0/1	0/1	0/1	0/1	0/1

NR, not report.

Table G Laboratory results

Study ID	Number	Leucocytes (×10⁹/L)	Lymphocytes (×10⁹/L)	Neutrophils (×10⁹/L)	Platelets (×10⁹/L)	Haemoglobin (×10⁹/L)	Albumin (g/L)	Alanine aminotransferase (U/L)	Aspartate aminotransferase (U/L)	Total bilirubin (μmol/L)	Blood urea nitrogen (mmol/L)	Creatinine (μmol/L)	Creatine kinase (U/L)	Lactate dehydrogenase (U/L)	Myoglobin (ug/L)	Procalcitonin (ng/mL)	CRP (mg/L)	Activated partial thromboplastin time (s)	Prothrombin time (s)	D-dimer (mg/L)
Deng 2020, (32)	2	4.83/5.08	3.37/2.89	NR	225/287	NR	NR	10.63/12.25	23.32/20.87	NR	NR	27.33/35.29	75.33/83.78	NR	NR	0.19/<0.05	12/<10	Normal/NR	Normal/NR	0.41/NR
Cai 2020, (33)	1	16.0	NR	NR	138	NR	NR	17	33	NR	NR	29	NR	NR	NR	0.07	15	Normal	Normal	0.58
Zhang 2020, (34)	1	9.68	NR	NR	494	113	NR	NR	NR	NR	NR	NR	NR	NR	NR	0.073	5.66	NR	NR	NR
Chen 2020, (36)	1	7.52	NR	NR	183	108	Normal	Normal	Normal	Normal	15.9	224	NR	NR	NR	NR	NR	NR	14.3	Normal
Zeng 2020, (37)	1	7.66	NR	NR	399	132	Normal	Normal	Normal	Normal	Normal	Normal	NR	NR	NR	0.08	<0.75	NR	NR	NR
Wang 2020, (39)	1	16.09	1.38	13.97	278	NR	Normal	20	31	Normal	Normal	Normal	NR	NR	NR	NR	NR	Normal	Normal	Normal
Quan 2020, (40)	1	9.1	4.5	NR	234	138	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	NR	<0.499	NR	NR	NR
Xiong 2020, (41)	2	6.0/6.2	2.56/3.73	2.18/1.72	301/252	112/117	43.2/Normal	58.5/Normal	83.5/Normal	NR/Normal	Normal	Normal	NR/Normal	NR	NR	NR/0.05	0.36/7.81	Normal	Normal	Normal
Liu 2020, (45)	6	2.96/6.49/5.48/3.04/3.95/1.8	1/1.19/1.25/1.7/0.87/0.36	1.3/3.15/2.54/0.66/2.85/0.27	203/272/256/191/153/165	104/120/113/118/115/120	40/45.2/43.6/45.4/44.3/42.3	6/14/11/23/43/15	45/30/42/64/36/37	NR/4/4.2/2.7/3.6/5.4	NR	33/34/22/29/23/30	29/50/77/148/71/82	384/197/476/375/297/280	NR	NR	38.4/21/23.32/11.8/58.79/6.84	NA/32.2/43.7/41/34/41.5	NR/13.2/12.8/11.9/12.3/12.5	0.59/0.22/0.78/0.22/0.74/0.38
Zhao 2020, (48)	1	3.9	NR	NR	NR	NR	Normal	Normal	Normal	Normal	496	Normal	Normal	Normal	Normal	0.06	Normal	NR	NR	NR
Zhang 2020, (51)	2	5.94/8.98	NR	NR	255/324	111/112	NR/NR	12.48/13.11	45.48/63.94	NR	5.16/5.30	21.6/17.90	30.48/102.53	318.37/540.33	NR	0.85/0.23	0.05/0.04	Normal	Normal	Normal
Liu 2020, (52)	1	3.78	1.86	1.68	149	138	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Xiao 2020, (53)	1	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Chan 2020, (55)	1	6.5	2.8	3.2	197	146	49.1	23.9	28.2	3.6	5.6	51	78	194	NR	NR	0.2	34.0	13.1	NR
Kam 2020, (56)	1	Normal	Normal	Normal	Normal	Normal	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Park 2020, (57)	1	4.08	NR	NR	251	135	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	< 0.04	NR	NR	NR
Liu 2020, (59)	4	Decreased/Normal/Normal/Normal	Increased/Increased/Normal/Normal	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	Normal/Normal/Normal/Increased	NR	NR	NR
Wang 2020, (60)	1	NR	2.43	NR	NR	NR	NR	NR	143	33	NR	NR	479	NR	NR	NR	NR	NR	NR	NR
Ji 2020, (62)	2	11.82/6.6	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	34.64/3.49	NR	NR	NR
Xing 2020, (66)	3	7.3/9.6/6.0	5.4 /5.2 /4.9	1.2 /3.6/1.7	333.0 /411.0/186.0	332.0/359.0/332.0	NR	NR	NR	NR	NR	22.8/28.3/53.4	73.2/88.6/91.0	264.3/NR/194.0	NR	0.23/0.21/0.73	<0.8/<5.0/10.5	NR	NR	860.0/230.0/190.0
Qian, (70)	1	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Sun, (73)	8	1.65/14.95/9.19/8.32/8.8/10.6/3.85/7.6	0.69/1.96/2.7/6.41/3.6/4.04/1.7/2.8	0.78/11.63/5.7/1.27/3.5/5.9/1.9/3.8	140/68/145/666/247/515/154/250	83/90/103/111/123/150/159/136	NR	58/66/36/100/55/9/16/8	37/27/33/41/16/14/14/16	11.8/20.4/16.5/12.4/5.3/7.8/8.1/8.1	NR	27.1/43.4/21.3/15/24.8/64.5/58/72.1	15/20,702/33/148/262/106/72/77	394/888/282/891/471/370/209/187	NR	0.18/17.16/0.05/0.08/0.11/0.04/0.09/0.05	6.48/57.9/103/0.75/27.02/1/9.9/0.5	NR	NR	0.47/40.34/3.07/NR/NR/NR/0.23/0.44
Dong, (74)	2	NR/normal	NR/normal	NR/normal	NR/normal	NR/normal	NR/normal	NR/normal	NR/normal	NR/normal	NR/normal	NR/normal	NR/normal	NR/normal	NR/normal	NR/normal	NR/normal	NR/normal	NR/normal	NR/normal
Le, (77)	1	10.23	8.3	1.19	230	112	NR	34.8	59.9	NR	NR	36.5	NR	327	NR	0.08	0.32	NR	NR	NR
Tang, (80)	1	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR

NR, not report; NA, not applicable.