Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

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Supplementary Appendix (20-05073)

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Methods

Study Design and Participants

This was an observational study that recruited children and adolescents confirmed to have severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection treated at the Wuhan Children's Hospital located in Wuhan, the epidemic center of this novel infection. The Wuhan Children's Hospital is the only designated hospital for treating patients under 16 years of age with SARS-CoV-2 infection in Wuhan assigned by the central government. Children with known contact with individuals having confirmed or suspected SARS-CoV-2 infection would undergo confirmatory testing. All the children tested positive for SAR-CoV-2 were recruited in this study. This study included children presented to our hospital between January 28 to February 26, 2020. The natural history and clinical outcomes were monitored up to March 8, 2020. This study was approved by the institutional ethics board of the Wuhan Children's Hospital (Approval number WHCH 2020003). Informed consent was obtained from parents or legal guardian of each patient.

Data Collection

Data from the medical records were extracted by members of the research team and were checked by two independent researchers. Epidemiological data were collected through interviews with the patients, their parents and legal guardians. Clinical presentation, comorbidities, laboratory results, radiological findings including chest radiographs and computed tomographic (CT) scans, modalities of treatment (oxygen therapy, intensive care support, use of antiviral or antibacterial agents) and outcomes were extracted from the medical records and entered into our clinical record form for subsequent analyses.

Real-Time Reverse Transcription Polymerase Chain Reaction Assay for SARS-CoV-2

Nasopharyngeal swabs from suspected children younger than 2 years of age and throat swabs from children 2 years or older were obtained for detection of SAR-CoV-2 RNA. After collection, the swabs were transported to the laboratory within 2 hours in a collection tube with 150 microliter virus preservative medium. RNA from the respiratory specimens was extracted with the High Pure Viral Nucleic Acid Kit (Zhongzhi, Wuhan, China). The extracted nucleic

acids were tested for SAR-CoV-2 using real-time reverse transcription polymerase chain reaction (RT-PCR) assay as described previously. [1,2] In brief, the following sequences of SARS-CoV-2 were adopted for the RT-PCR assays: forward primer 5′-TCAGAATGCCAATCTCCCCAAC-3′; reverse primer 5′-AAAGGTCCACCCGATACATTGA-3′;
probe 5′CY5-CTAGTTACACTAGCCATCCTTACTGC-3′BHQ1.
Amplifications were initially done at 50°C for 15 min and subsequently at 95°C for 3 min, followed by 45 cycles of 95°C for 15 s and 60°C for 30 s.

Results

The age distribution of patients and their respective diagnoses (asymptomatic infection, upper respiratory tract infection, pneumonia) were summarized in Table S1. The median ages of asymptomatic patients, patients with upper respiratory infections (URTI), and patients with pneumonia were 9.6, 3.9, and 5.9 years, respectively. The laboratory results of all children were summarized in Table S2. Laboratory results were expressed as median (interquartile range) or n (%). The 6 (3.5%) patients with lymphopenia either had URTI or pneumonia. Figure S1 shows abnormalities of the chest CT images from representative patients.

Table S1. Age distribution of infected children and their respective diagnoses

	n (%) or median (IQR)			
	All patients (n = 171)	**Asymptomatic infection (n=27)**	**Upper respiratory tract infection (n = 33)**	**Pneumonia (n =111)**
Age -years				
Median (IQR)	6.7 (2.0-9.8)	9.6 (7.6-12.6)	3.9 (1.4-8.4)	5.9 (1.2-9.3)
<1	31 (18.1)	0	6 (18.2)	25 (22.5)
1-5	40 (23.4)	1 (3.7)	12 (36.4)	27 (24.3)
6-10	58 (33.9)	14 (51.9)	10 (30.3)	34 (30.6)
11-15	42 (24.6)	12 (44.4)	5 (15.2)	25 (22.5)

Table S2. Laboratory results of 171 infected children and their respective diagnoses

Measures	All patients (n = 171)	Diagnosis		
		Asymptomatic infection (n=27)	Upper respiratory tract infection (n = 33)	Pneumonia (n =111)
Blood routine (unit; normal range)				
White blood cell count ($\times 10^9$/L; 5.5-12.0)	6.8 (5.5-8.2)	7.0 (6.1-8.1)	6.9 (5.5-8.6)	6.6 (5.3-8.2)
<5.5	45/171 (26.3)	1/27 (3.7)	9/33 (27.3)	35/111 (31.5)
Neutrophil count ($\times 10^9$/L; 1.1-3.9)	2.5 (1.8-3.7)	3.4 (2.9-3.9)	2.5 (1.7-3.9)	2.3 (1.6-3.5)
Lymphocyte count ($\times 10^9$/L; 1.2-6.0)	2.9 (2.2-4.4)	2.8 (2.4-3.3)	3.1 (2.6-4.6)	2.9 (1.9-4.5)
<1.2	6 (3.5)	0(0)	1(3.0)	5(4.5)
Hemoglobin (g/L; 110.0-149.0)	126.0 (118.0-135.0)	132.0 (125.0-135.0)	128.0 (121.0-138.0)	125.0 (115.0-133.0)
Infection biomarkers (unit; normal range)				
Procalcitonin (pg/ml; 0-46) *	50 (40-80)	40 (30-50)	50 (40-80)	60.0 (40-90)
>46	105 (64.0)	10 (40.0)	22 (68.8)	73 (68.2)
C-reactive protein (mg/L; 0.0-10.0)	4.0 (1.3-8.0)	2.0 (1.0-4.0)	4.0 (1.3-6.8)	4.0 (1.7-9.0)
>10	33 (19.7)	2 (7.4)	4 (12.1)	27 (24.3)
Blood biochemistry (unit; normal range)				
Lactate dehydrogenase (U/L; 120.0-300.0)	246 (207-305)	215 (181-254)	243 (215-323)	254 (216-329)
Alanine aminotransferase (U/L; 7-45)	15 (11-27)	13 (11-20)	13 (11-28)	16 (11-28)
Increased	21 (12.3)	1 (3.7)	4 (12.1)	16 (14.4)
Aspartate aminotransferase (U/L; 10-50)	30 (24-42)	25 (20-31)	30 (24-46)	32.0 (24-46)
>50	25 (14.6)	0 (0)	5 (15.2)	20 (18.0)
Alkaline phosphatase (U/L; 42.0-220.0)	198.0 (156.0-245.0)	202.0 (126.0-239.0)	186.0 (165.0-217.0)	198.0 (158.0-256.0)
Creatinine (μmol/L; 27.0-62.0)	33.9 (26.1-42.7)	42.6 (36.4-47.1)	29.0 (23.3-39.7)	31.7 (25.8-42.0)
Blood urea nitrogen (mmol/L; 2.9-7.1)	4.1 (3.3-4.8)	4.7 (3.6-5.5)	4.1 (3.4-4.4)	4.1 (3.1-4.8)

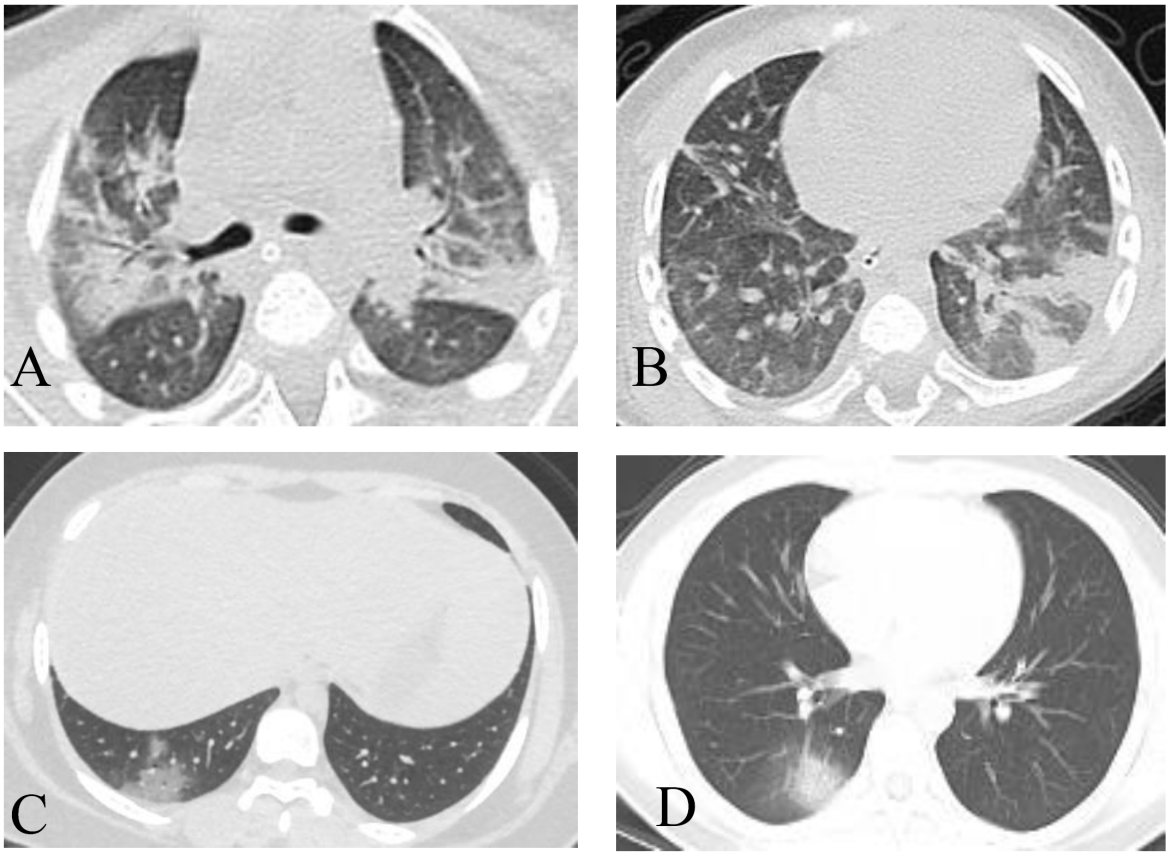
Coagulation markers (unit; normal range)				
Fibrinogen (g/L; 2.0-4.0)	2.1 (1.8-2.7)	1.8 (1.8-2.0)	2.2 (1.9-2.8)	2.1 (1.8-2.8)
D-dimer (mg/LFEU; 0.0-0.6) #	0.2 (0.2-0.4)	0.2 (0.1-0.2)	0.2 (0.2-0.4)	0.4 (0.3-1.0)
>0.6	21 (14.1)	0 (0)	4 (16.0)	17 (17.5)
Prothrombin time (s; 10.2-13.4)	10.9 (10.6-11.3))	10.9 (10.6-11.1)	10.8 (10.6-11.5)	11.0 (10.6-11.3)
Thrombin time (s; 14.0-21.0)	18.4 (17.7-19.2)	18.5 (17.9-19.0)	18.2 (17.7-18.7)	18.5 (17.7-19.4)
Electrolytes (unit; normal range)				
Potassium (mmol/L; 3.5-5.3)	4.8 (4.3-5.2)	4.4 (4.3-4.7)	4.8 (4.3-5.6)	4.8 (4.4-5.2)
Sodium (mmol/L; 137.0-147.0)	139.1 (138.0-140.5)	140.4 (139.5-141.6)	139.1 (138.2-140.2)	138.9 (137.6-140.1)
Chloride (mmol/L; 99.0-110.0)	101.3 (99.7-103.0)	100.5 (99.9-102.9)	101.8 (99.7-103.1)	101.1 (99.5-103.0)

*Procalcitonin was available from 164 patients (25 patients with asymptomatic infection, 32 patients with upper respiratory tract infection, 107 patients with pneumonia)

#D-dimer was available from 149 patients (27 patients with asymptomatic infection, 25 patients with upper respiratory tract infections and 97 patients with pneumonia.

Figure S1. Chest CT scan images of representative patients.

Representative chest CT scan images from patients with different severity of the infection. Bilateral ground glass opacities in a thirteen-month old boy with severe pneumonia requiring ICU care (A, B). Chest CT scan image from a 14-year old girl showing basal infiltrates (C). Chest CT scan image from a 15-year old asymptomatic boy showing ground glass opacity in the right posterior lung field.



Author Contributions

XL, GW, KS, and SX conceptualized the study design. XL, JZ, YYL, DL, HD, JS, GW, and SX analysed the data with input from JS, XP, YY, ZL, YX, YW, FZ, SB, LZ, HX, YL, CW, JQ, WZ, HL, YY. XL, JZ, GW wrote the first draft with all authors providing critical feedback for subsequent revisions of the manuscript. All authors read and approved the final report.

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Declaration of interests

The authors have no competing interests to declare.

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