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Research note

Childhood COVID-19: a multicentre retrospective study

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ABSTRACT

Objectives: To investigate the clinical and epidemiological characteristics of paediatric patients with coronavirus disease-19 (COVID-19).

Methods: Paediatric patients diagnosed with COVID-19 between January 15 and March 15, 2020, from seven hospitals in Zhejiang Province, China, were collected retrospectively and analysed.

Results: Thirty-two children with COVID-19, ranging in age from 3 months to 18 years, were enrolled. Family aggregation occurred in 87.5% of infant and preschool-aged children (7/8), and also school-aged children (14/16), but in only 12.5% (1/8) of adolescents ($p < 0.05$, $p < 0.001$). Most of these patients had mild symptoms: mainly fever (20/32) followed by cough (10/32) and fatigue (4/32). The average durations of viral RNA in respiratory samples and gastrointestinal samples were 15.8 d and 28.9 d, respectively. Detox duration in faeces decreased with age: 39.8 d, 27.5 d and 20.4 d in infants and preschool children, school children, and adolescents respectively ($p_{0-6, -18} < 0.01$, $p_{0-6, -14} < 0.05$). Pneumonia was found in 14 children, but there was no statistical significance in the incidence of pneumonia between different age groups. Thirty patients were treated with antiviral drugs, and all patients were stable and gradually improved after admission.

Conclusions: Most children with COVID-19 had a mild process and a good prognosis. More attention should be paid to investigation of household contact history in the diagnosis of COVID-19 in young children. Viral RNA lasts longer in the gastrointestinal system than in the respiratory tract, especially in younger children. **Z. Chen, Clin Microbiol Infect 2020;26:1260.e1–1260.e4**

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Introduction

The newly emerging infectious disease, coronavirus disease-19 (COVID-19), has now become prevalent all over the world, causing widespread concern. Children are a special group with

immature immune systems and respiratory systems which make the disease process and manifestation different from those in adults [1,2]. To summarize the clinical experience in the diagnosis and treatment of paediatric COVID-19, we retrospectively collected

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and analysed the clinical data of 32 confirmed paediatric patients from seven hospitals in Zhejiang province, eastern China.

Methods

Data collection

We collected 36 children with COVID-19. Of these, four patients were excluded due to incomplete clinical data. Clinical characteristics and laboratory examinations as well as radiological and microbiological findings were recorded and analysed. This study was approved by the ethics committee of the Children's Hospital, Zhejiang University School of Medicine (EC approval number: 2020-IRB-032).

Real-time reverse-transcriptase polymerase chain reaction (RT-PCR)

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) was detected with primers and probes targeting the ORF1ab and N genes by RT-PCR assay according to the manufacturer's instructions (Shanghai Huirui Biotechnology Co. Ltd, China). A cycle threshold value (Ct value) of ≥ 40 was defined as a negative test. A Ct value < 37 of both target genes was defined as a positive case; a medium load or only one target gene with a Ct value ≤ 37 was considered to be a suspected case and required confirmation by retesting.

Data analysis

A one-way non-parametric analysis of variance (ANOVA) followed by an unpaired Student's t-test were conducted for comparisons of the parameters between groups. LSD test was used for pairwise comparison between multiple data. Enumeration data were subjected to the χ^2 test or Fisher's exact test. All analyses were performed using IBM SPSS Statistics 20 software. Statistical significance was accepted at $p < 0.05$.

Results

Demographic data

Thirty-two children with an average age of 9.5 years (range 3 months to 18 years) were enrolled (see Table 1). All the children were previously healthy.

Epidemiological and clinical data

COVID-19 tended to be clustered in families; 22 of the 32 children had at least one family member a confirmed COVID-19 patient. This phenomenon of family aggregation occurred in 87.5% of infant and preschool-aged children (7/8), 87.5% of school-aged children (14/16), and only 12.5% of adolescents (1/8) (Fisher's exact test, $p_{0-6, -18} < 0.05$, $p_{-14, -18} < 0.001$). The clinical manifestations of these patients were generally mild (see Table 1).

Viral RNA detection

We collected sequential viral RNA information from 25 patients. Detailed information is presented in Fig. 1. The average duration of viral RNA in respiratory samples (nasopharyngeal swab or sputum) was 15.8 d (range 1–29 d). The average durations in infants and preschool children, school children and adolescents were 12.67 ± 8.26 d, 16 ± 7.93 d and 18 ± 8.49 d, respectively, without statistical difference.

Seventeen children were tested for viral RNA in faeces or anal swabs; viral RNA was present with an average duration of 28.9 ± 11.81 d, with the longest time of 65 d in the youngest case, a 3-month-old girl. Interestingly, the duration of viral RNA in faeces decreased with age, being 39.8 d in infants and preschool children, 27.5 d in school-age children, and 20.4 d in adolescents (LSD test, $p_{0-6, -18} < 0.01$, $p_{0-6, -14} < 0.05$) (Fig. 1A).

Nine urine tests in two children and five serum tests in one case were all negative.

When looking more deeply into the Ct value of virus RNA, as is shown in Fig. 1 (B and C) the viral RNA load in respiratory samples gradually decreased until it became negative, while the viral RNA in faeces tended to fluctuate around a certain value before being cleared.

Chest imaging findings

All patients underwent imaging examinations, including seven chest film and 25 computed tomography scans (CTs). Pneumonia was found in 14 children (Table 1). No statistical significance in the percentage of pneumonia was found among different age groups ($p > 0.05$). When grouped by gender, a slightly higher proportion of boys had pneumonia, but this did not reach statistical difference (10/21 versus 4/11).

Table 1
Clinical features of 32 children with confirmed coronavirus disease-19 (COVID-19)

	All patients	0–6	–14	–18
Number (male/female) (n)	32 (21/11)	8 (3/5)	16 (13/3)	8 (5/3)
Family aggregation n (%)	22 (68.75%)	7 (87.5%)	14 (87.5%)	1 (12.5%)
Classification				
Mild (n)	18	5	7	6
Common (n)	14	3	9	2
Severe (n)	0	0	0	0
Critical (n)	0	0	0	0
Fever				
Number (n)	20	5	9	6
~38°C (n)	11	2	5	4
~39°C (n)	9	3	4	2
>39°C (n)	0	0	0	0
Cough (n)	10	3	3	4
Fatigue (n)	4	1	2	1
Diarrhoea (n)	3	1	2	0
WBC (mean \pm SE) (/L)	6.69 \pm 3.07	8.83 \pm 3.71	6.02 \pm 2.73	6.19 \pm 2.23
Proportion of pneumonia in imaging n (%)	14 (43.75%)	3/8 (37.5%)	9/16 (56.25%)	2/8 (25.0%)

WBC, white blood cell count.

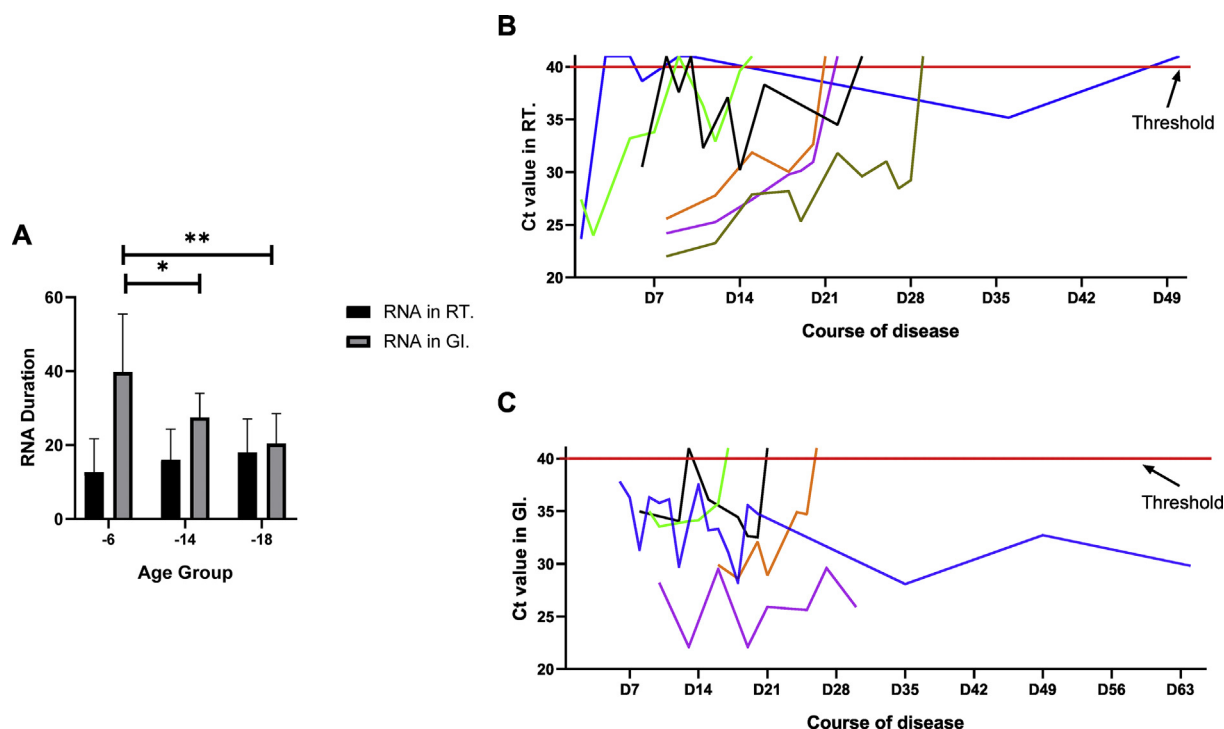


Fig. 1. Comparison of respiratory (RT) and gastrointestinal (GI) samples for the detection of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) RNA. (A) RNA duration in respiratory and digestive tracts between different age groups. (B) The dynamic change of SARS-CoV-2 RNA in the respiratory tracts of six typical patients (different colour for each patient). (C) The dynamic change in SARS-CoV-2 RNA in the digestive tracts of five typical patients (different colour for each patient).

Treatment and outcome

Thirty patients were treated with antiviral drugs, including recombinant interferon (24/30, 80%), lopinavir/ritonavir (15/30, 50%), arbidol (10/30, 33.33%), oseltamivir phosphate (4/30, 13.33%) and ribavirin (3/30, 10%). Oseltamivir phosphate was used only in the early course and for a short period.

Additionally, traditional Chinese medicine was used in seven children and probiotics were used in five children. Four patients received antibiotics because of suspected bacterial infection. No glucocorticoids or intravenous immunoglobulin (IVIG) were used.

All patients were stable and gradually improved after admission. No severe or critical case occurred. The average length of hospital stay was 21.29 d (range 5–32 d).

Discussion

Early clinical investigations suggested that COVID-19 is prevalent predominantly in adults [3,4], with only a small percentage of paediatric patients. According to the latest analysis, the proportion of children under 20 years of age with COVID-19 was only 2.1%, including 0.9% in the 0–10-year age group and 1.2% in the 10–20-year age group [5]. The first confirmed paediatric case of COVID-19 was a 10-year-old boy from a case-gathering family in Shenzhen, Guangdong Province, on January 15, 2020 [1]. Since then, more and more paediatric patients have been reported. The youngest infected case reported so far was 36 h after birth [6].

Here, we collected and analysed data on 32 COVID-19 children from seven hospitals in Zhejiang province. In our study, 22 of these patients (68.75%) had at least one family member a confirmed COVID-19 patient. This phenomenon of family aggregation occurred in 87.5% of infant, preschool-aged children and school-aged children, and in only 12.5% of adolescents. This result can be explained by the limited range of activities of young children. It also

highlights the importance of family aggregation history in the clinical diagnosis of paediatric COVID-19, especially for younger children [7].

As in the severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS) and avian influenza A H7N9 outbreaks [8,9], symptoms of paediatric COVID-19 were generally mild [3,10]. Only one fatal paediatric case has been reported so far in China, and the overall severe and critical rate was around 5.8% [11], much lower than that in adults (18.5%) [12].

The dynamics of SARS-CoV-2 *in vivo* is a focus of research at present. In our study, it was found that the average viral RNA duration in respiratory samples (pharyngeal swab or sputum) was 15.8 d, much longer than the clinical symptoms. Further analysis revealed that gastrointestinal samples (faeces or anal swabs) had a much longer virus duration (28.9 d) than respiratory samples. Interestingly, the duration of virus in the digestive tract decreased with age: 39.8 d in infants and preschool children, 27.5 d in school-age children, and 20.4 d in adolescents. The youngest patient (3 months) showed the longest duration of faecal viral RNA (65 d). This happens to coincide with the fact that the viral RNA shedding in children is much longer than that in adults [13,14]. It is necessary to determine whether there are active virus particles in the faeces.

As in other studies [13,15], no positive result for viral RNA was found either in serum or in urine.

In summary, COVID-19 in most paediatric cases was characterized by mild symptoms and transient fever with good prognosis. More attention should be paid to investigation of household contact history in the diagnosis of COVID-19 in young children. Viral RNA lasts longer in the gastrointestinal system than in the respiratory tract, especially in younger infants.

A limitation of this study is that only 32 patients were involved. Even though we found some interesting phenomena, the limitations of the data prevent us from drawing firm conclusions.

Author contributions

ZC, LT and YZ contributed equally to this work. The study was conceived by QS, JF and ZC. Data collection was performed by CH, WW, LH, HX, ZX, YC, SY, XW, LW, YL, XZ, XT and YZ. Statistical analysis and draft writing were performed by LT and YZ under the leadership of ZC. All authors have read and approved the manuscript.

Transparency declaration

The authors declare that they have no conflict of interests. This programme was supported by Zhejiang University special scientific research fund for COVID-19 prevention and control (2020XGZX0081).

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