



Clinical characteristics of pediatric inpatients infected with the SARS-CoV-2 Omicron variant—a retrospective observational cohort study

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Background: The children infected with the Omicron variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are at risk of progressing to severe disease. Clinical characteristics treatment measures and prognosis of these special age group of patients have not been completely understood which necessitate more researches. This study sought to analyze the clinical characteristics of children infected with the Omicron variant to provide evidences for the prevention, diagnosis and treatment of the Omicron variant infection in children.

Methods: The subjects of this study included children hospitalized for the Omicron variant at Tianjin Binhai Hospital in November 2022. The data were collected from the electronic medical record system, and the clinical characteristics of the children were analyzed. The primary endpoints included the clinical presentation, laboratory tests, virological characteristics, treatment regimen, and clinical prognosis of the patients.

Results: A total of 49 patients were enrolled, of whom 32 (65.3%) were male. The patients had a median age of 10 (interquartile range, 6–11) years, and 34.7% of the patients received 2 or more coronavirus disease 2019 (COVID-19) vaccines. The main clinical manifestations of the patients were fever (79.6%) and cough (24.5%), with a maximum temperature of 42 °C and a median temperature of 39 (interquartile range, 38.4–39) °C. The proportions of neutrophils and C-reactive protein were elevated by 50.0% and 25.0%, respectively. The total percentages of white blood cells and thrombocytopenia were 12.5% and 6.3%, respectively. D-dimer was examined in 6 cases, and was elevated to 1.77 µg/mL in 1 case (16.7%), and normal in 5 cases. The liver function, kidney function, and coagulation of 9 (100%) patients were all normal. After the anti-virus, anti-inflammatory response, antipyretic, and traditional Chinese medicine treatments, all the children were cured and discharged from the hospital. There were no severe cases.

Conclusions: The main manifestations of children infected with the SARS-CoV-2 Omicron variant were fever and cough. Some children had a high fever, nasal congestion, runny nose, gastrointestinal symptoms, and rash. A proportion of 12.5% of patients have a white blood cell count less than $4 \times 10^9/L$, and 6.3% have thrombocytopenia. The prognosis of the child was favorable after treatment with antiviral, antipyretic, and traditional Chinese medicine.

Keywords: Novel coronavirus infection; Omicron variant; children; clinical features

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Introduction

On November 24, 2021, the World Health Organization (WHO) announced a novel variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), B.1.1.529, which was first detected in samples collected in November 2021 in Botswana and South Africa and is known as the Omicron variant (1). Compared to the original novel coronavirus strains including Alpha, Beta, Gamma and Delta, at least 59 variants of the Omicron variant were identified. Most of these variants are located in key regions of the nucleic acid mediating viral recognition, binding, and the invasion of host cells. These genetic information changes enhance the infectivity and immune evasion ability of the Omicron variant (2), and the clinical consequence is a spreading rate significantly faster than the earlier variants (3).

In the first week of January 2022, a total of 149 countries reported to the WHO >15 million new cases of Omicron, the largest number of cases reported in a week since the beginning of the outbreak (4). After the emergence of the Omicron variant, the number of infections and hospitalizations of children has continued to increase, suggesting that the Omicron variant may have a higher

risk of infection and transmission than previous strains in children (5). On January 8, 2022, the first case of childhood infection with the Omicron variant was reported in Tianjin, China, and within 1 month, >100 children were confirmed to be positive for the infection (5). Apparently, the clinical characteristics of the disease and fatality rates of children infected with the Omicron variant are severe as compared with adults. The reason seems to be that in this special age group of patients, the cellular immunity and humoral immune functions are not yet mature, and the children infected with Omicron variant are at risk of progressing to severe disease. Clinical characteristics treatment measures and prognosis of these special age group of patients have not been completely understood. These observations justify the need to conduct further research on the effects of Omicron infection in children (6,7).

This study analyzed the clinical characteristics of children infected with the Omicron variants to provide an evidence-based reference to potentially utilize for improving diagnosis and treatment, based on the obtained effects of treatment, and help in formulating scientific epidemic prevention and control strategies. We present this article in accordance with the STROBE reporting checklist (available at <https://tp.amegroups.com/article/view/10.21037/tp-23-292/rc>).

Highlight box

Key findings

- The main manifestations of children infected with the SARS-CoV-2 Omicron variant were fever and cough. The prognosis of the child was favorable after treatment with antiviral, antipyretic, and traditional Chinese medicine.

What is known and what is new?

- In November 2021, the Omicron variant of COVID-19 was announced by the World Health Organization. The children infected with Omicron variant are at risk of progressing to severe disease.
- The Omicron variant is more contagious than the previous variants in adults and children.

What is the implication, and what should change now?

- Most of the children infected with the Omicron variant recovered and were discharged after symptomatic treatments, such as antiviral and antipyretic treatments, with a good clinical prognosis.

Methods

Study design

This cohort study was conducted at Tianjin Binhai Hospital affiliated to Peking University. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Tianjin Binhai Hospital (No. WZX-EC-KY2023001) and individual consent for this retrospective analysis was waived.

Study population

The study subjects comprised children who were hospitalized for novel coronavirus infection at the Binhai Hospital of Tianjin University General Hospital (Tianjin Designated Hospital for Novel Coronavirus Infection) from November 19 to November 30, 2022, a period when

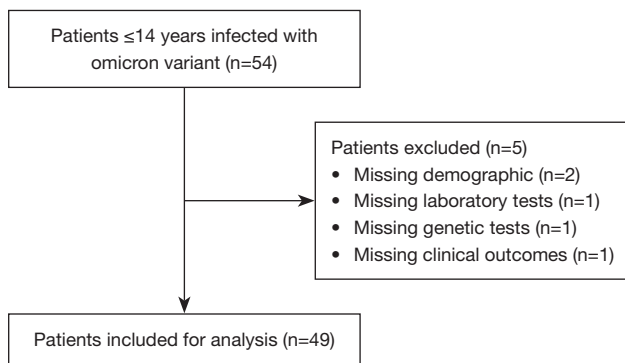


Figure 1 The patients inclusion flowchart.

the cases infected with Omicron variant surged in China. To be eligible for inclusion in this study, the patients had to meet the following criteria: (I) age ≤ 14 years; (II) positivity for Omicron variant infection as determined by positive results for SARS-Cov2 RNA in real-time PCR assay of a nasopharyngeal swab and the gene sequencing results. Patients with missing data including demographic characteristics, laboratory and/or genetic tests, or clinical outcomes were excluded from the study.

Study endpoints

The primary endpoints included prognosis, incidence of severe illness and mortality rate. The secondary endpoints included symptoms and abnormalities in laboratory test parameters. The prognosis was assessed based on symptoms, COVID-19-related complications, and disease progression.

Data collection

The following data were collected from the electronic medical record system and video case consultations: gender, age, clinical manifestations (fever, cough/sputum, dry throat/sore throat, nasal congestion/runny nose, rash or nausea/vomiting), routine laboratory indicators (blood routine, liver and kidney function, coagulation function, D-dimer, C-reactive protein, and procalcitonin), the viral nucleic acid cycle threshold (Ct) value, nucleocapsid (N) gene value, and open reading frame (ORF) gene value of the specimens taken from the respiratory tract, requirement for intensive care, the information regarding treatment regimen, and clinical outcomes. The data were collected independently by 2 investigators and the discordances were

solved by consensus.

Statistical analysis

The Shapiro-Wilk test was used to detect the normality of continuous variables. The normally distributed continuous variables are expressed as the mean \pm standard deviation, and the non-normally distributed continuous variables are expressed as the median [interquartile range (IQR)]. The categorical variables are expressed as the count (percentage). All the statistical analyses were performed with IBM[®] SPSS[®] Statistics Software (version 22) (SPSS Inc., USA).

Results

Baseline characteristics and major clinical manifestations of the included patients

The patient inclusion flowchart was showed in *Figure 1*. A total of 49 patients were included in the study, of whom 32 (65.3%) were male. The patients had a median age of 10 (IQR, 6–11) years, and 10.0%, 55.3% and 34.7% of patients received 0, 1 or more 2 doses of vaccine, respectively. Patients with a temperature higher than 38.5 °C received antipyretic treatment. The main clinical manifestations of the patients were fever (79.6%) and cough (24.5%), with a maximum temperature of 42 °C and a median temperature of 39.0 (IQR, 38.4–39.0) °C. The baseline characteristics and clinical manifestations of the included patients are shown in *Table 1*.

Virological indicators and routine laboratory test results

The Ct values of the coronavirus disease 2019 (COVID-19) were tested. The N gene values and ORF gene values of 10 randomly selected patients were tested, and the patients had mean values of 27.3159 ± 3.4035 and 28.4992 ± 2.2006 , respectively.

In this study, the routine laboratory tests were performed in 16 patients who developed high fever. The results indicated that the proportions of neutrophils and C-reactive protein elevated in 50% and 25% of these patients, respectively. The total percentages of white blood cells (WBCs) and thrombocytopenia were 12.5% and 6.2%, respectively. The laboratory results are set out in *Table 2*. On a total of 6 patients examined for D-dimer, 1 patient had elevated D-dimer (1.77 $\mu\text{g/mL}$), while the other

Table 1 Demographic features and major clinical manifestations of the included patients

Features	All patients (n=49)
Male	32 (65.3)
Age (years)	10 [6–11]
Vaccination ≥ 2 times	17 (34.7)
Fever (≥ 37.3 °C)	39 (79.6)
Cough/sputum	12 (24.5)
Dry throat/sore throat	3 (6.1)
Nasal congestion/runny nose	2 (4.1)
Rash	4 (8.2)
Nausea/vomiting	4 (8.2)

The data are expressed as number (percentage) or median [interquartile range].

Table 2 Routine laboratory tests results

Item	All patients (n=16/49, 32.65%)
Total number of white blood cells $< 4 \times 10^9/L$	2 (12.5)
The elevated percentage of neutrophils	8 (50.0)
The decreased absolute lymphoid values	5 (31.3)
Thrombocytopenia	1 (6.3)
C-reactive protein elevated	4 (25.0)

The data are expressed as number (percentage).

5 patients had normal D-dimer. Notably, the liver function, kidney function, and coagulation of these 6 patients were all normal.

Patient treatment regimens and clinical outcomes

Ibuprofen was given to 32 febrile children when their body temperature was > 38.5 °C; the indications for antipyretic drugs were appropriately adapted for children with a history of convulsions. Dexamethasone anti-inflammatory therapy was given to 2 children with persistent high fevers and achieved good results. Depending on symptoms, signs and laboratory results, 26 patients were treated with Lianhuaqingwen capsule [ingredients: Weeping Forsythia Capsule, Japanese Honeysuckle Flower, Ephedra Herb (honey-fried), Bitter Apricot Seed (stir-baked), Gypsum, Isatis Root, Male Fern Rhizome, Heartleaf Houlttuynia

Herb, Cablin Patchouli Herb, Rhubarb, Bigflower Rhodiola Root, Menthol, and Liquorice Root.], 4 with Child Chiqiao Qingre Granules [ingredients: *Forsythia suspensa*, light fermented soybeans, mint, mustard, gardenia (stir fried), rhubarb, artemisia annua, red peony, betel nut, magnolia officinalis, *Scutellaria baicalensis*, and *Pinellia ternata*], 10 with oseltamivir antiviral therapy, 2 with intravenous fluids, and 2 with Cefixime for anti-infection. All the 49 patients were cured and discharged and no cardiovascular or pulmonary complications were observed during the subsequent 3 months of follow-up.

Discussion

In this retrospective study, the clinical features of 49 children infected with the Omicron variant were observed. The main clinical manifestations of the patients were fever and cough. About one-third of the included children had been vaccinated > 2 times. The laboratory tests results indicated that the neutrophil ratio increased in more than half of the patients. Most of the included patients had no abnormalities in liver and kidney function and coagulation indicators. After treatment with the antipyretic, antiviral, and traditional Chinese medicine such as Lianhuaqingwen capsule and Child Chiqiao Qingre Granules, most of the patients had favorable outcomes, and no children required any period of admission to intensive or intermediate care unit.

According to the literature, children are generally considered susceptible to COVID-19. A study in Shenzhen, China, showed that the secondary infection rate (7.1–7.4%) among the close contacts of children was similar to that of adults (8). Childhood infection rates at the beginning of the COVID-19 epidemic ranged between 2–9.0%, and surveillance data from Europe, the United States (U.S.), and South Africa for the Omicron variant showed a marked increase in childhood infection rates compared to those reported in the initial epidemic (9,10). Data from U.S. studies suggest that patients aged < 18 years accounted for 17% of the total number of patients during the Omicron variant epidemic, and the incidence of children < 5 years of age was 6 to 8 times higher than that during the Delta variant epidemic (11,12).

Data from the early epidemic [2020] in China showed that 13.2% of the children admitted to a hospital in Wuhan had asymptomatic infections, and only 2.2% of these children had severe and critical infections (8). The most common symptoms were cough (44.5%) and fever (43.4%) (8).

Notably, during the Omicron variant epidemic, data from the U.S. indicated that up to 37.6% of children were asymptomatic (13). In addition, children infected with the Omicron variant had a significantly lower risk of developing severe disease than those with the Delta variant (14). The evidence from these studies suggests that children are generally susceptible to the Omicron variant, but they could have milder symptoms after infection and a lower risk of developing severe disease.

Chen *et al.* (15) retrospectively analyzed the clinical features of 22 children infected with the Omicron variant in 2022. Among the 22 children, there were 7 cases of fever, 4 cases of sore throat, 2 cases of fatigue, and 17 cases of cough and sputum. After antiviral and traditional Chinese medicine treatments, all 22 children recovered and were discharged from the hospital, and there were no severe cases. Gui *et al.* (16) analyzed the clinical manifestations, laboratory tests, lung computed tomography imaging, nucleic acid detection, clinical classification, vaccination, and diagnosis and treatment efficacy of 94 children with the Omicron strain infection. Only 34 (36.2%) of the 94 patients had been vaccinated, and the clinical manifestations mainly included fever and respiratory symptoms (60.6%). Other symptoms included nasal congestion, a runny nose, vomiting, diarrhea (6.4%), and a skin rash (3.2%). Interestingly, 76.6% of the patients were asymptomatic or had mild symptoms. After diagnosis and subsequent treatments with traditional Chinese medicine and anti-infection treatments, the children were all cured. In a recently published study, Qi *et al.* (17) analyzed the clinical data of 19 children infected with the SARS-CoV-2 Omicron variant. Of the 19 children, 8 (42.1%) with mild or ordinary clinical symptoms had been vaccinated, and there were no severe cases. The most common symptoms were cough (100%) and fever (63%). The WBC count and lymphocyte count of the children was normal, and no obvious abnormalities were observed in the platelet count, procalcitonin, liver and kidney functions of the patients. All 19 children were cured and discharged after receiving antiviral and symptomatic treatments. The total percentages of thrombocytopenia were 6.3% in our study. The pathophysiology of thrombocytopenia in COVID-19 is hypothetically caused by the impaired hematopoietic stem cells and megakaryocyte maturation due to an increase of specific inflammatory cytokines (18,19). One patient had elevated D-dimer in our study. D-dimer level is one of the measures used in patients to detect thrombosis. Studies have reported that an increase in D-dimer concentration in the early stages of COVID-19

was associated with poor prognosis. Measuring the level of D-dimer and coagulation parameters from the early stage of the disease can also be useful in controlling and managing of COVID-19 disease (20).

The above results are consistent with those of our study, which indicated that the Omicron variant is more contagious than the previous variants in adults and children. However, the pathogenicity of the Omicron variant is reduced compared to the original strain, for which the main clinical manifestations are fever, cough, nasal congestion, a runny nose, and gastrointestinal symptoms. Most of the patients recovered and were discharged after symptomatic treatments, such as antiviral and antipyretic treatments, with a good clinical prognosis. Notably, traditional Chinese medicine formulas and proprietary Chinese medicines could play a supporting role in the treatment of the Omicron variant infection in children.

Limits of the study

This retrospective observational study had several limitations. First, because this is a retrospective study, the risk of information bias and selective bias may increase. However, we pre-defined strict inclusion and exclusion criteria in an effort to control bias. Second, a small sample size may lead to insufficient data available for meaningful statistical analysis. Third, imaging and laboratory tests are not comprehensive. Fourth, the study lacked a non-Omicron variant control group. Future studies with large sample sizes, control groups and more clinical information are warranted.

Conclusions

The main clinical manifestations of children infected with the SARS-CoV-2 Omicron variant were fever and cough, and some children had high fever, sore throat, nasal congestion, a runny nose, vomiting, conjunctivitis, skin rash, and other symptoms. Laboratory examination results show that some children have decreased platelets and WBCs, especially lymphocytes. Most of the children had a good prognosis after antiviral, antipyretic, and treatments with traditional Chinese medicine.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at <https://tp.amegroups.com/article/view/10.21037/tp-23-292/rc>

Data Sharing Statement: Available at <https://tp.amegroups.com/article/view/10.21037/tp-23-292/dss>

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://tp.amegroups.com/article/view/10.21037/tp-23-292/coif>). The 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. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Tianjin Binhai Hospital (No. WZX-EC-KY2023001) and individual consent for this retrospective analysis was waived.

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