Clinical characteristics and predictors of delayed discharge among children with SARS-CoV-2 Omicron variant infection

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Abstract. The present study investigated the epidemiology and clinical characteristics of infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Omicron variant and determined the risk factors for delayed discharge or release from isolation for pediatric patients in Quanzhou, China in 2022. There were 145, 254 and 23 patients in the asymptomatic, mildly symptomatic and moderately symptomatic categories, respectively. The proportion of pediatric patients in the moderately symptomatic category increased with increasing age. No child aged <1 year and 9.02% of patients aged 13-18 years were in the moderately symptomatic category. The proportion of patients with asymptomatic infection did not differ significantly by vaccination status. The median days until the first negative conversion of viral RNA was 11 days, and the median hospitalization duration was 16 days. Most symptoms appeared in the upper respiratory tract. Notably, ~33.23% of patients showed elevated aspartate aminotransferase levels. C-reactive protein and interleukin-6 (IL-6) levels, and lymphocyte counts were consistently lower in asymptomatic patients than those in in symptomatic patients. Adjusted logistic regression analyses indicated that IL-6 levels and time to the first negative conversion of viral RNA were independent risk factors for delayed discharge. The area under the curve of the regression model for predicting delayed discharge was 0.760. In conclusion, these results could facilitate the formulation of global epidemic prevention policies for pediatric patients.

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Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has infected >496 million people and caused ~6 million deaths worldwide, posing a serious threat to life (1). Since its emergence, SARS-CoV-2 has been constantly evolving and mutating, and less virulent but more infectious strains have emerged, thereby bringing challenges to the prevention and control of the COVID-19 pandemic (2). The Omicron variant of SARS-CoV-2 emerged in November 2022 (3) and spread globally at an unprecedented rate. Compared with previous variants, the Omicron variant is more infectious, is associated with a lower hospitalization rate, and causes significantly less severe symptoms and complications (4,5). The manifestations of SARS-CoV-2 infection in children differ from those in adults, and children tend to experience milder symptoms than adults (6). Most children either experience mild symptoms or are asymptomatic, and serious complications, such as acute respiratory distress syndrome, multisystem inflammatory syndrome and long-term sequelae, are rare (7-11). However, the

current understanding of the epidemiology, clinical characteristics and effectiveness of vaccination in children infected with the Omicron variant is limited. In addition, investigation into the factors related to the length of hospital stay and quarantine can alleviate the admission burden in designated hospitals; however, there is currently limited information available on the risk factors for delayed discharge or release from quarantine in children infected with the Omicron variant. Since the outbreak of the Omicron variant in Quanzhou, China in March 2022, all patients infected with the variant have been admitted to designated hospitals or mobile cabin hospitals for quarantine and treatment, regardless of their age or symptoms. This measure has facilitated a comprehensive and detailed analysis of the epidemiology and clinical characteristics of infection with the SARS-CoV-2 Omicron variant, and the risk factors for delayed discharge or release from quarantine in children, particularly infants and toddlers, in this region. The present study may provide a reference for the prevention of COVID-19 in children.

Materials and methods

Data source. The present study analyzed data on children who were admitted to two designated COVID-19 hospitals (Chengdong Clinic and Infectious Disease Clinic, which are both affiliated to the Fujian Medical University Affiliated Quanzhou-First Hospital, Quanzhou, China) and three mobile cabin hospitals (Huoweishan, Nan'an and Dongshi Mobile Cabin Hospitals, which are managed by Fujian Medical University-Affiliated Quanzhou First Hospital) between 13 March and 6 May 2022. All patients were ≤18 years old at the time of admission. They were subsequently divided into asymptomatic, mildly symptomatic and moderately symptomatic groups according to the diagnostic criteria specified in the Diagnosis and Treatment Protocol for COVID-19 (Trial Version 9) (12). Patients were defined as asymptomatic if they did not show any relevant symptoms, mildly symptomatic if they had mild symptoms but no pneumonia manifestations on imaging, and moderately symptomatic if they showed both symptoms and pneumonia manifestations on imaging. Mild symptoms included fever, dry cough, sore throat, fatigue, sputum production, myalgia, coryza, poor appetite, diarrhea and a decreased sense of smell.

The discharge criteria were as follows: Body temperature 35-37.3˚C for >3 consecutive days, significant alleviation of respiratory symptoms, significant improvement of acute exudative lesions on pulmonary imaging, and cycle threshold values for N and ORF genes being consistently ≥35 in two consecutive quantitative PCR (qPCR) tests performed ≥24 h apart. All data were collected from the hospital registry system, and at least two positive PCR test results, performed by the Quanzhou Center for Disease Control and Prevention (Quanzhou, China), were required for confirmation of the diagnosis.

Data detection. The white blood cell (WBC) count, neutrophil count, neutrophil percentage, lymphocyte count, lymphocyte percentage, red blood cell count, hemoglobin level and platelet count were measured using an automatic hematology analyzer (Coulter LH750 analyzer; Beckman Coulter, Inc.), dye solution (lot number: A2079), hemolysis agent (lot number: ZG801013) and diluent (lot number: ZG801004) (all supplied by SYSMEX CORPORATION). Albumin, total bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase and γ-glutamyl transpeptidase levels were measured using an automated chemistry analyzer (AU5811; Beckman Coulter, Inc.). The prothrombin time (PT), and fibrinogen and D-dimer levels were measured using an automated blood coagulation analyzer (ACL-TOP700; Instrumentation Laboratory Company; Werfen Life Group). Procalcitonin (PCT) levels were measured using an automated chemiluminescence immunoassay system (MINI VIDAS®; bioMérieux Clinical Diagnostics_ and a reagent (lot number: 25-0015) provided by Star Child Medical Technology Co., Ltd. For SARS-CoV-2 RNA load detection, total RNA was extracted from 200 μl liquid throat swab and sputum samples according to the manufacturer's instructions (nucleic acid extraction or purification reagent; lot number: TQ-BG-008-96D-96; Xi'an Tianlong Science & Technology Co., Ltd.) with the NP968-C system (Xi'an Tianlong Science & Technology Co., Ltd.). Subsequently, 5 μl RNA mixture was transferred to a PCR tube and mixed with a 20 μl amplification system (17 μl ORF1ab/N reaction solution + 3 μl enzyme mixture) for reverse transcription (lot number: 5205051; Da'an Gene Co., Ltd.). The expression levels were quantified via quantitative PCR using Novel Coronavirus 2019-nCoV Nucleic Acid Detection Kit (Fluorescent PCR) (Da'an Gene Co., Ltd.) and QuantStudio5 (Applied Biosystems; Thermo Fisher Scientific, Inc.) under the following conditions: Reverse transcription at 50˚C for 15 min; initial denaturation at 95˚C for 15 min; 45 cycles at 94˚C for 15 sec and 55˚C for 45 sec. Values were calculated as cycle quantification (Cq) values, and Cq ≤40 was considered a positive result.

Statistical analyses. All statistical analyses were performed using SPSS 23.0 (IBM Corp.). Continuous data are shown as medians and interquartile ranges (IQRs), and categorical variables are reported as frequencies and percentages. Categorical variables were compared between groups using the χ^2 test or Fisher's exact test. Continuous variables were compared using the Kruskal-Wallis test for multiple comparisons. Univariate and multivariate logistic regression models were used to explore factors associated with delayed discharge or release from quarantine. Receiver-operating characteristic (ROC) curve analysis was used to evaluate the diagnostic value. $P<0.05$ was considered to indicate a statistically significant difference.

Results

Epidemiological characteristics. In total, 422 children infected with the Omicron variant were recruited, including 145 (34.4%) with asymptomatic infections, 254 (60.2%) with mildly symptomatic infections, and 23 (5.45%) with moderately symptomatic infections (Table I). None of the participants had severe or critical infection. There were 214 male participants and 208 female participants. Symptom severity did not differ significantly according to sex (P=0.438). Among the male participants, 69 (32.2%) had asymptomatic infection, 135 (63.1%) had mild symptoms, and 10 (4.7%)

Table I. Demographic and clinical characteristics of 422 children infected with the SARS-CoV-2 Omicron variant.

Characteristic	Total no. of patients (n=422)	No. of asymptomatic patients (n=145)	No. of mildly symptomatic patients (n=254)	No. of moderately symptomatic patients (n=23)	P-value
Sex					0.438
Male	214 (50.71)	69 (32.24)	135 (63.08)	10 (4.68)	
Female	208 (49.29)	76 (36.54)	119 (57.21)	13 (6.25)	
Age groups					0.276
≤1 year	41 (9.72)	11 (26.83)	30 (73.17)	0	
2-6 years	109 (25.83)	39 (35.78)	66 (60.55)	4 (3.67)	
7-12 years	128 (30.33)	51 (39.84)	71 (55.47)	6 (4.69)	
13-18 years	144 (34.12)	44 (30.56)	87 (60.42)	13 (9.02)	
Symptoms and signs					
Fever	184 (43.60)	0	170 (92.39)	14 (7.61)	0.556
Dry cough	121 (28.67)	0	111 (91.76)	10 (8.24)	0.984
Sore throat	51 (12.09)	0	47 (92.16)	4 (7.84)	>0.999
Fatigue	48 (11.37)	0	45 (93.75)	3 (6.25)	0.78
Expectoration	36 (8.53)	0	29 (80.56)	7 (19.44)	0.023
Muscle soreness	27 (6.40)	0	27 (100)	0	0.201
Runny nose	23 (5.45)	0	20 (86.96)	3 (13.04)	0.641
Loss of appetite	15 (3.55)	0	15 (100)	0	0.473
Diarrhea	11 (2.61)	0	11 (100)	0	0.378
Loss of taste and smell	8 (1.90)	0	8 (100)	0	0.495
Stuffy nose	6 (1.42)	0	5 (83.33)	1 (16.67)	0.408
Headache	5 (1.18)	0	5 (100)	0	0.646
Dizziness	4 (0.95)	0	4 (100)	0	0.706
Shortness of breath	4 (0.95)	0	4 (100)	0	0.706
Aversion to cold	3 (0.71)	0	3 (100)	0	0.770
Chest tightness	3 (0.71)	0	3 (100)	0	0.770
Vomiting	2 (0.47)	0	2 (100)	0	0.841
Palpitation	2 (0.47)	0	1 (50)	1 (50)	0.159
Bloating	1 (0.24)	0	1 (100)	0	0.917
Median respiratory rate, beats/min (IQR)	20 (20-21)	20 (20-21)	20 (20-22)	20 (20-21)	0.390
Median blood oxygen saturation, % (IQR)	98 (98-99)	98 (98-99)	98 (98-99)	99 (98-99)	0.868
Median length of hospital stay, days (IQR)	16 (13-19)	15 (12-18.5)	16 (13-19)	18 (15-20)	0.004
Median time to first negative SARS-CoV-2 PCR result, days (IQR)	11 (8-14)	10 (6-13)	11 (11-14)	12 (10-16)	0.010
Vaccination status					0.186
Unvaccinated	90 (21.33)	28 (31.11)	61 (67.78)	1 (1.11)	
1 dose	24 (5.69)	7 (29.17)	15 (62.50)	2 (8.33)	
2 doses	279 (66.11)	104 (37.38)	156 (55.91)	19 (6.81)	
3 doses	20 (4.74)	5 (25.00)	14 (70.00)	1 (5.00)	
Unsure	9 (2.13)	1 (11.11)	8 (88.89)	0	
Contact history					0.451
Yes	167 (39.57)	56 (33.53)	99 (59.28)	12 (7.19)	
No	105 (24.88)	42 (40.00)	59 (56.19)	4 (3.81)	
Unsure	150 (35.55)	47 (31.33)	96 (64.00)	7 (4.67)	

Unless otherwise specified, the data are expressed as the number of cases (%). Categorical variables were compared between groups using the χ^2 test or Fisher's exact test. Continuous variables were compared using the Kruskal-Wallis test for multiple comparisons. IQR, interquartile range; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

had moderate symptoms. The median age of the participants was 9 years (IQR: 4.75-14 years). The youngest participant was 19 days old, and the oldest was 18 years old. Overall, 41 (9.7%) participants were aged <1 year, 109 (25.8%) were aged

2-6 years, 128 (30.3%) were aged 7-12 years, and 144 (34.1%) were aged 13-18 years. The proportion of moderately symptomatic patients increased with increasing age, ranging from 0 among children aged <1 year to 13 (9.0%) among children aged 13-18 years. The majority of patients (n=323, 76.5%) had received at least one dose of vaccine, 90 (21.3%) were unvaccinated, and the vaccination status was unclear in the remainder. The proportion of patients with asymptomatic infection did not differ significantly by vaccination status (P=0.186). In addition, 167 (39.57%) patients had a clear history of contact and most were infected by household transmission. As all patients were local residents, this outbreak is believed to have been spread primarily by community transmission.

Clinical manifestations. Among the 422 infected patients, only one showed a comorbidity, namely diabetes mellitus. The top ten clinical manifestations were fever (184 cases, 43.6%), dry cough (121 cases, 28.7%), sore throat (51 cases, 12.1%), fatigue (48 cases, 11.4%), expectoration (36 cases, 8.5%), muscle soreness (27 cases, 6.4%), runny nose (23 cases, 5.45%), loss of appetite (15 cases, 3.6%), diarrhea (11 cases, 2.6%), and loss of taste and smell (8 cases, 1.9%). The median time to first negative SARS-CoV-2 PCR test result was 11 days (IQR: 8-14 days) overall. The time to first negative SARS-CoV-2 PCR test result increased significantly with increasing severity (10 days in the asymptomatic group, 11 days in the mildly symptomatic group, and 12 days in the moderately symptomatic group; P=0.01). The median length of hospital stay was 16 days (IQR: 13-19 days) overall. The median length of hospital stay was significantly shorter in the asymptomatic group (15 days; IQR: 12-18.5 days) than in the mildly symptomatic (16 days; 13-19 days; P=0.043) and moderately symptomatic (18 days; 15-20 days; P=0.012) groups. The difference in the length of stay between the mildly symptomatic and moderately symptomatic groups was not statistically significant (P=0.216).

Laboratory and imaging results. In total, 330 infected patients underwent routine blood tests (Table II). Most patients had a normal WBC count, but 30 (9.1%) had a decreased WBC count ($<3.5x10^9$/l). The lymphocyte count and lymphocyte percentage were decreased, and the monocyte percentage was increased, as disease severity increased. Only a minority of patients (n=35, 10.61%) showed an abnormal C-reactive protein (CRP) level and erythrocyte sedimentation rate, and 54 (16.36%) showed a mildly elevated PCT level. Among the 259 patients whose interleukin-6 (IL-6) levels were measured, almost half (n=123, 47.49%) had an elevated IL-6 level over the maximum detection value (-5,000 pg/ml). This level rapidly decreased or returned to normal after 2 days of comprehensive treatment (including rest, psychological support and traditional Chinese medicine treatment).

Among the patients who had the relevant tests 7.5% (24/322) developed hypoalbuminemia, 2.5% (8/322) had elevated ALT levels, 33.23% (107/322) had elevated AST levels, 3.8% (12/319) had elevated creatine kinase levels, and 47.34% (151/319) had elevated lactate dehydrogenase (LDH) levels. In addition, the D-dimer level was increased in 24.6% (73/297) of patients, and the PT was mildly elevated in 28.2% (82/291) of patients. The proportion of patients with mildly elevated PT was the highest in the moderately symptomatic group, followed by the mildly symptomatic and asymptomatic groups. The notable elevation in serum albumin levels was observed in symptomatic patients compared with that in asymptomatic patients.

Of the 298 children who underwent complete lung computed tomography (CT) on admission, only 23 exhibited clinical manifestations on the CT images. Specifically, seven (30.4%) patients showed bilateral involvement, eight (34.8%) showed ground-glass opacities, and seven showed patchy opacities combined with ground-glass opacities. In addition, one patient each showed a patchy opacity, streaky opacity, ground-glass nodule, patchy opacity combined with ground-glass and streaky opacities, patchy opacity combined with a streaky opacity, patchy opacity combined with streaky and nodular opacities, and ground-glass opacity combined with nodular opacity (4.34%).

Clinical treatment. All children were treated with traditional Chinese medicine. Five patients were also infected with influenza A or B, and were therefore prescribed oseltamivir. In addition, aerosol inhalation was required for four patients, and aerosol inhalation combined with arbidol was required for three patients (usual prescription: Interferon-α 50 μg nebulized inhalation two times a day (bid), arbidol 200 mg three times a day; oseltamivir: ≤15 kg, 30 mg bid; 1-23 kg, 45 mg bid; 24-40 kg, 60 mg bid; and >40 kg, 75 mg bid). All patients recovered well and met the discharge criteria.

Risk factors for delayed discharge or release from quarantine. To explore the risk factors for delayed discharge or release from quarantine, patients with incomplete laboratory results were excluded from the analysis. Subsequently, using the median length of hospital stay of 16 days as the threshold, patients were divided into a control group (length of hospital stay ≤16 days, n=179) and an observation group (length of hospital stay >16 days, n=152). Univariate logistic regression analysis showed that age, time to first negative SARS-CoV-2 PCR test result, lymphocyte count, IL-6 and LDH were related to delays in discharge or release from quarantine. Multivariate logistic regression analysis showed that only the IL-6 level and time to first negative SARS-CoV-2 PCR test result were risk factors for delayed discharge or release from quarantine (Table III). Subsequently, based on the regression coefficient, a binary logistic regression model was established as follows: Y=0.002 x IL-6 + 0.228 x (time to the first negative SARS-CoV-2 PCR test result)-2.381.

The ROC curve was used to evaluate the diagnostic value of the model. The ROC analysis showed that the area under the curve for predicting delayed discharge was 0.760, with a 95% confidence interval of 0.704-0.817 (Fig. 1). When the cut-off value was set to 0.527, the sensitivity and specificity of the model for predicting delayed discharge were 63.0 and 77.4%, respectively. Therefore, through this model, it may be possible to predict which patients can be discharged early and which patients are likely to stay longer, helping to speed up bed turnover and relieve the pressure of hospitalization.

Discussion

The results of the present study suggested that children of all ages are susceptible to the Omicron variant of SARS-CoV-2,

Table II. Laboratory and imaging results for 422 children infected with the severe acute respiratory syndrome coronavirus 2 Omicron variant on admission.

Item	Asymptomatic patients (n=145)	Mildly symptomatic patients (n=254)	Moderately symptomatic patients (n=23)	P-value
WBC count, x10^9/l	6.11 (4.86-8.18) (n=86)	5.86 (4.48-7.65) (n=223)	4.79 (3.48-6.45) (n=21)	0.075
NE count, x10^9/l	2.60 (1.72-3.83) (n=86)	2.58 (1.74-4.12) (n=223)	2.59 (2.07-4.36) (n=21)	0.887
NE, %	44.90 (31.23-58.40) (n=86)	49.60 (35.30-61.40) (n=223)	55.40 (42.55-65.80) (n=21)	0.029
LY count, x10^9/l	2.55 (1.79-3.63) (n=86)	1.90 (1.32-3.150) (n=223)	1.34 (0.97-1.98) (n=21)	<0.001
LY, %	41.85 (28.35-56.05) (n=86)	37.00 (25.00-50.90) (n=223)	28.7 (20.2-37.6) (n=21)	0.007
NE count/LY count	1.06 (0.55-2.01) (n=86)	1.35 (0.69-2.34) (n=223)	1.90 (1.19-3.02) (n=21)	0.009
Monocyte count, x10^9/l	0.52 (0.39-0.74) (n=86)	0.61 (0.45-0.83) (n=223)	0.67 (0.33-0.84) (n=21)	0.041
Monocytes, %	8.50 (6.60-10.45) (n=86)	10.70 (8.20-13.4) (n=223)	10.40 (8.25-13.30) (n=21)	<0.001
RBC count, x10^{12}/l	4.68 (4.44-4.93) (n=86)	4.72 (4.41-4.98) (n=223)	4.72 (4.52-5.17) (n=21)	0.545
Hemoglobin, g/l	128.5 (122.0-137.3) (n=86)	130.0 (121.0-139.0) (n=223)	133.0 (124.5-144.0) (n=21)	0.485
PLT count, x10^9/l	270.0 (222.5-330.0) (n=86)	253.0 (199.0-300.0) (n=223)	270.0 (199.0-333.5) (n=21)	0.143
CRP, mg/l	0.50 (0.47-2.40) (n=85)	2.16 (0.49-4.62) (n=223)	2.63 (0.51-4.18) (n=21)	<0.001
PCT, ng/ml	0 (0-0.06) (n=74)	0.05 (0-0.09) (n=204)	0 (0-0.07) (n=21)	0.012
ESR, mm/h	11.50 (7.00-19.75) (n=64)	12.00 (8.00-22.00) (n=187)	9.50 (5.00-17.25) (n=18)	0.436
Interleukin-6, pg/ml	2.59 (0-7.29) (n=63)	6.73 (3.15-30.29) (n=178)	6.19 (3.39-14.86) (n=18)	<0.001
Ferritin, ng/ml	46.30 (30.25-70.80) (n=40)	65.90 (31.90-98.80) (n=125)	53.30 (41.10-94.40) (n=13)	0.192
Albumin, g/l	43.60 (41.55-45.15) (n=85)	44.45 (43.03-46.10) (n=216)	44.30 (42.75-45.90) (n=21)	0.022
TBIL, μmol/l	7.40 (5.95-9.50) (n=85)	7.45 (5.53-9.98) (n=216)	7.50 (6.55-11.10) (n=21)	0.547
ALT, U/l	12.00 (9.50-15.00) (n=85)	14.00 (11.00-18.00) (n=216)	11.00 (9.00-14.50) (n=21)	0.005
AST, U/l	27.00 (21.00-36.00) (n=85)	30.00 (23.25-39.00) (n=216)	24.00 (20.00-30.00) (n=21)	0.005
ALP, U/l	218.0 (165.0-262.5) (n=85)	202.5 (130.3-253.8) (n=216)	230.0 (115.0-291.5) (n=21)	0.313
GGT, U/l	13.0 (11.0-15.0) (n=85)	14.0 (11.0-17.0) (n=216)	14.0 (12.5-16.0) (n=21)	0.060
Urea, mmol/l	4.14 (3.33-4.89) (n=84)	4.12 (3.52-4.94) (n=216)	3.52 (3.07-4.30) (n=21)	0.053
Creatinine, μmol/l	38.9 (31.3-49.00) (n=84)	43.2 (32.13-55.93) (n=216)	44.90 (32.70-53.65) (n=21)	0.153
Glucose, mmol/l	4.42 (4.07-4.69) (n=84)	4.57 (4.19-5.03) (n=216)	4.67 (4.26-5.29) (n=21)	0.029
Potassium, mmol/l	4.38 (4.07-4.67) (n=84)	4.14 (3.93-4.47) (n=216)	4.25 (3.87-4.60) (n=21)	0.006
Sodium, mmol/l	138.1 (137.1-139.0) (n=84)	137.8 (136.2-139.4) (n=216)	138.40 (134.9-139.55) (n=21)	0.639
Uric acid, μmol/l	320.0 (256.0-366.5) (n=84)	322.0 (263.0-384.8) (n=216)	319.0 (261.5-370.5) (n=21)	0.764
Creatine kinase, U/l	85.0 (65.0-115.0) (n=83)	99.0 (70.0-136.0) (n=215)	87.0 (58.5-103.0) (n=21)	0.032
Creatine kinase-MB, U/l	23.3 (18.2-30.8) (n=83)	23.70 (17.9-31.2) (n=215)	18.3 (13.4-24.7) (n=21)	0.054
Lactate dehydrogenase, U/l	237.0 (195.0-311.0) (n=83)	249.0 (208.0-307.0) (n=215)	230.0 (198.5-281.0) (n=21)	0.507
Troponin I, ng/ml	0.001 (0.001-0.001) (n=49)	0.001 (0.001-0.002) (n=155)	0.001 (0.001-0.001) (n=17)	0.608
PT, sec	11.90 (11.33-12.38) (n=72)	12.40 (11.60-13.30) (n=200)	13.00 (12.40-14.30) (n=19)	<0.001
D-dimer, mg/l FEU	0.24 (0.17-0.42) (n=78)	0.34 (0.19-0.55) (n=199)	0.28 (0.20-0.41) (n=20)	0.036
Fibrinogen, g/l	2.69 (2.34-3.00) (n=72)	2.98 (2.60-3.32) (n=200)	3.00 (2.60-3.72) (n=19)	<0.001

Unless otherwise specified, the data are expressed as the median (IQR). n represents the number of children who have been tested for this item. Continuous variables were compared using the Kruskal-Wallis test for multiple comparisons. ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; FEU, fibrinogen equivalent units; GGT, γ-glutamyl transpeptidase; IQR, interquartile range; LY, lymphocyte; NE, neutrophil; PCT, procalcitonin; PLT, platelet; PT, prothrombin time; RBC, red blood cell; TBIL, total bilirubin; WBC, white blood cell.

with no significant sex difference, which is consistent with the findings of a previous study (13). In the present study, 76.5% patients were vaccinated against COVID-19. In the vaccinated group, 93.19% patients were either asymptomatic or mildly symptomatic, with only 6.8% being moderately symptomatic, and none showed severe or critical illness. Vaccination has been reported to be less effective against the Omicron variant (14,15). In the present study, there were no significant differences in disease severity according to COVID-19 vaccination status or the number of vaccine doses received. According to the analysis of the UK Health Security Agency, the hospitalization rate in children <1 year old increased rapidly after they were infected with the Omicron variant, accounting for 42.4% of all hospital admissions (16). Furthermore, during the initial outbreak in

Table III. Univariate and multivariate logistic regression analyses of risk factors for delayed discharge from the hospital in children infected with the SARS-CoV-2 Omicron variant.

	Univariate analysis		Multivariate analysis	
Variable	OR (95% CI)	P-value	OR (95% CI)	P-value
Age	1.06 (1.02-1.10)	0.003	1.02 (0.95-1.09)	0.596
Time to first negative SARS-CoV-2 PCR test result	1.27 (1.19-1.36)	<0.001	1.26 (1.16-1.36)	<0.001
Lymphocyte count	0.84 (0.73-0.96)	0.012	1.06 (0.85-1.34)	0.596
Interleukin-6	1.00 (1.00-1.00)	0.017	1.00 (1.00-1.01)	0.043
Lactate dehydrogenase	0.996 (0.993-0.999)	0.013	0.998 (0.993-1.00)	0.438

CI, confidence interval; OR, odds ratio; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

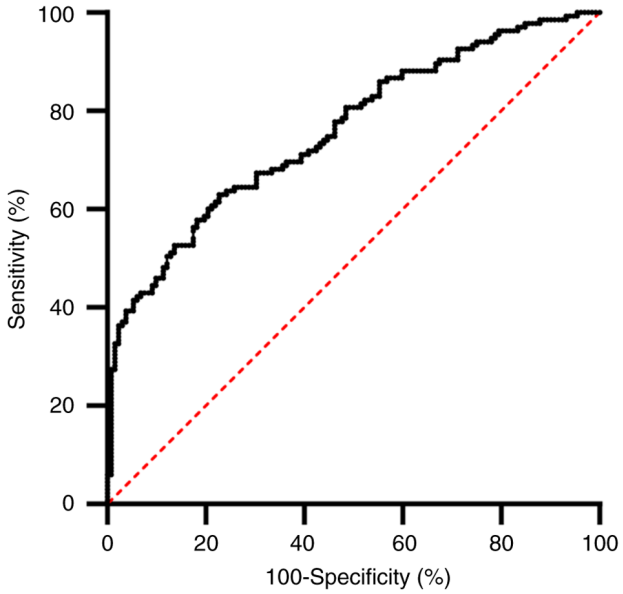

Figure 1. Receiver-operating characteristic curve of the Y model.

Wuhan in 2019, nearly half of the critically ill children infected with SARS-CoV-2 were <1 year old (17). By contrast, in the present study, children <1 year old only accounted for 9.72% of all patients, and were either asymptomatic or mildly symptomatic. However, the proportion of moderately symptomatic cases gradually increased with increasing age, reaching up to 9.02% among patients aged 13-18 years. This result suggested that as the patient's immune system gradually improved, the corresponding stronger immune response may have contributed to the severity of Omicron infection.

The three most common symptoms of Omicron infection in children were fever, dry cough and sore throat. Less common symptoms included fatigue, myalgia, coryza, diarrhea, and the loss of taste and smell. In addition, acute upper respiratory tract symptoms were dominant, whereas symptoms involving the lung parenchyma, such as dyspnea and wheezing, were rare. Relatively milder symptoms in children infected with the Omicron variant were noted as compared with those of the previous variants (18,19), which was also supported by the finding that only a small number of patients (7.72%) showed ground-glass opacities of the lungs on CT images. This suggests that symptoms caused by Omicron infection are concentrated in the upper respiratory tract (20). In addition, the proportion of children with fever in the present study was substantially lower than that in a previous study (43.60 vs. 76.1%) (21).

The present study revealed that the lymphocyte count and lymphocyte percentage were inversely associated with disease severity, suggesting that the lymphocyte count decreased with disease progression. This is consistent with the significant decrease in the lymphocyte count in critically ill patients (22). However, whether the decline in lymphocytes was a result of decreased production or increased consumption requires further clinical evaluation. Up to 53% of patients with COVID-19 have been reported to exhibit abnormal levels of liver enzymes (23). By contrast, the present study found that the risk of liver injury in children with Omicron variant infection was low, as only 2.48% of the participants had elevated ALT levels. Of the participants with elevated ALT levels, 33.23% also had elevated creatine kinase-MB levels, probably due to myocardial injury. A growing number of studies have shown that COVID-19 can lead to myocardial damage, which is more pronounced in children with multisystem inflammatory syndrome. This myocardial damage is associated with major adverse events, but not mortality (24-26). In addition, the AST levels of participants in the present study were only slightly elevated, and they rapidly returned to the normal level once symptoms were alleviated. This finding suggests that myocardial involvement does not cause pathological damage. Although an endocardial biopsy can provide pathological evidence that helps confirm the diagnosis, it was not performed in the current study due to its invasiveness (24). It is worth mentioning that the rate of Omicron-induced myocardial injury in adults is extremely low. Therefore, the relatively high incidence of myocardial damage among study participants may be related to their underdeveloped cardiac function (27). Another study reported that COVID-19 can activate the thrombus inflammatory pathway, and consequently, cause abnormal coagulation (28). In the present study, the PT and fibrinogen levels of the asymptomatic, mildly symptomatic and moderately symptomatic patients increased in a stepwise manner, although the differences according to symptom severity were not marked. In addition,

the patients showed no bleeding tendency. Moreover, most patients experienced rapid symptom relief and rarely experienced digestive symptoms, such as loss of appetite; as a result, few patients had serum albumin levels below the lower limit of normal. In addition, compared with in asymptomatic patients, symptomatic patients generally eat more high-quality proteins (such as milk and beef) to fight the infection.

Previous studies have shown that the dysregulation of cytokine release is the clinical cause of severe SARS-CoV-2 infection (29,30), and as the main inflammatory cytokine, IL-6 is significantly elevated in critically ill patients (31). The univariate and multivariate logistic regression analyses showed that the IL-6 levels and time to first negative SARS-CoV-2 PCR test result were independent risk factors for delayed discharge. The combination of IL-6 levels and time to first negative SARS-CoV-2 PCR result effectively predicted when patients could be discharged. These results could help clinicians make clinical decisions as early as possible and relieve the pressure on admission in designated hospitals. A study by Choi *et al* (32) of children hospitalized with COVID-19 in South Korea included some children with severe and critical disease. The investigators revealed that the presence of complex comorbidities was significantly associated with severe COVID-19 and that neurological disease was a significant predictor of severe disease.

The present study has some limitations. First, the duration of fever in some patients could not be calculated, as the onset of their fever could not be determined. Second, the incubation period could not be estimated because of the lack of access to the children's contact history. Third, because the patients were not followed-up, the effect of the Omicron variant on the children's growth and development could not be evaluated. Fourth, the present study only collected data for patients in Quanzhou, whose symptoms were generally mild; therefore, the characteristics of the Omicron variant may not have been described comprehensively. Due to the lack of patients with severe disease and the small number of patients with moderate symptoms, the results should be interpreted with caution. Additionally, patients with moderate symptoms tended to be admitted to hospitals earlier than those with mild symptoms, and hence, the biochemical markers in their peripheral blood may not yet have peaked by the time they were measured. Studies that include patients with severe disease and larger numbers of patients with moderate disease are required to clarify the relationship between abnormalities measured on blood biochemistry and disease severity.

In conclusion, children were generally susceptible to the Omicron variant, regardless of their age and vaccination status, with no significant differences between male and female patients. Household transmission was the main source of infection, and vaccination showed a protective effect. The primary clinical manifestations of the Omicron variant included fever, dry cough and sore throat, whereas involvement of the lung parenchyma was rare. Compared with adults, children were more likely to develop myocardial damage after infection but could easily recover. The IL-6 level and time to first negative SARS-CoV-2 PCR test result were independent risk factors for delayed discharge.

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Availability of data and materials

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

Authors' contributions

YijuanZ, HZ, ZW, HH, YongjunZ and XY conceived and designed the study. WC, MZ and CC reviewed the literature and collected original patient information. YouxianZ, JX and KZ assessed the PCR screening results. JimingZ, BX, ZS and XZ analyzed the data. YijuanZ, HZ, ZW and HH performed the statistical analysis. YijuanZ, HZ, ZW, HH, YongjunZ and XY wrote the original draft. All authors read and approve the final manuscript. YongjunZ and XY confirm the authenticity of all the raw data.

Ethics approval and consent to participate

The present study was approved by the Ethics Committee of the Fujian Medical University-Affiliated Quanzhou First Hospital (Quanyilun 2020 No. 124). The parents/guardians of all participants provided written informed consent.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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