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Coronavirus Pandemic

Comparison of clinical and para-clinical characteristics between children and adults with the Omicron variant of COVID-19

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Abstract

Introduction: The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Omicron variant is associated with higher transmissibility, but lower disease severity, compared to some other variants. However, its exact pathogenicity among children is still largely unknown. This study was conducted to determine the differences in clinical characteristics between children and adults infected with this variant.

Methodology: A total of 327 Omicron-infected patients admitted to the First Affiliated Hospital of Nanchang University, between 7 December 2022 and 10 March 2023 were retrospectively evaluated. They were divided into two groups: children (0–18 years, n = 149) and adults (> 18 years, n = 178). Differences in clinical classifications, symptoms, imaging features, biochemical markers, and positive nucleic acid test durations were compared between the groups.

Results: Age had a significant impact on children in terms of clinical classifications ($p < 0.05$). Fever was the most common symptom among children (123/149), while coughing (151/178) was the most common among adults. The adults also had higher frequencies for pathological imaging features. The children had significantly higher white blood cell counts, and lymphocyte counts, while the adults had higher neutrophil percentages and C-reactive protein. Positive nucleic acid test durations were shorter among the children, compared to the adults. The children also had higher cumulative negative conversion and improvement rates ($p < 0.05$).

Conclusions: Overall, children with Omicron had milder clinical classifications, significantly different symptoms and biochemical indices, as well as lower occurrence of pathological imaging features and shorter positive nucleic acid test durations, compared to adults.

Key words: COVID-19; Omicron variant; clinical classifications; children; adult.

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Introduction

The Omicron variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), also known as B.1.1.529, was first identified on 24 November 2021, from Botswana, South Africa, and was classified as a variant of concern by the World Health Organization (WHO) on 26 November 2021, owing to its rapid spread worldwide [1]. Compared to previously reported SARS-CoV-2 variants such as Alpha and Delta, Omicron had higher transmissibility, but lower pathogenicity [2–4]. Coronavirus disease 2019 (COVID-19) caused by Omicron has been documented to have lower infectivity, occurrence, and severity among children, compared to adults. This lower infectivity has resulted in fewer children being tested, and consequently the actual number of infections within this population has been underestimated [5]. This underestimation has been magnified in light of the spread of the Omicron variant, as it has been associated with increased viral transmissibility, immune evasion, and re-infection risks [6], which, among children, have been reflected by increasing numbers of infected and/or hospitalized individuals. However, few clinical studies have been carried out to precisely examine the pathogenicity of the Omicron variant among children versus adults. This study aimed to fill that gap of knowledge by conducting a retrospective analysis of 149 children, and 178 adults, diagnosed with COVID-19 caused by the Omicron variant. We identified differences in patient characteristics and clinical outcomes, and found that significant differences in symptoms, as well as biochemical markers, were present between children and adults. Our aim was to investigate the similarities and differences in clinical features, auxiliary examination features, and clinical outcomes between children and adults with COVID-19 caused by the Omicron variant.

Methodology

Study population

The study included patients who were admitted to the First Affiliated Hospital of Nanchang University, with COVID-19 caused by the Omicron variant, between 7 December 2022 and 10 March 2023. The

patients were divided into 2 groups, based on their ages: "Children", defined as individuals 0–18 years old, and "Adults", defined as individuals > 18 years of age. Patient inclusion criteria were as follows: 1) meeting the diagnostic criteria for COVID-19, as defined in "Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Trial Version 10) [7], including a positive SARS-CoV-2 nucleic acid test; 2) the identified SARS-CoV-2 was highly homologous to the known Omicron variant sequence. All analyses were conducted in accordance with the Declaration of Helsinki, and were approved by the Ethics Committee at the First Affiliated Hospital of Nanchang University. Written informed consent was obtained from the patients, or from their parents/legal guardians if under the age of 16 years.

Clinical classification of COVID-19

The patients were diagnosed with COVID-19 in the following categories, based on the "Diagnosis and Treatment Protocol for Pneumonia", issued by the National Health Commission of the People's Republic of China [7], as follows: mild, moderate, severe, and critical. "Mild" was defined as having mild clinical symptoms, and no evidence of pneumonia in imaging analyses. "Moderate" was defined as having fever, pathological respiratory symptoms, and imaging characteristics associated with pneumonia. "Severe" was defined as an adult of any of the following characteristics: 1) shortness of breath, defined as breathing rate ≥ 30 times/min; 2) oxygen saturation of ≤ 93% at rest; 3) partial pressure of oxygen in arterial blood (PaO_2)/fraction of inspired oxygen (FiO_2) being ≤ 300 mmHg (1 mmHg = 0.133 kPa); or 4) significant lesion progression of > 50 lesions within 24–48 hours of lung imaging. Among the children, "Severe" was defined as a child with any of the following: 1) extremely high fever or persistent high fever for more than 3 days; 2) shortness of breath (< 2 months old, RR = 60/min; 2–12 months, RR = 50/min; 1–5 years old, RR = 40/min; > 5 years old, RR = 30/min), except the effects of fever and crying; 3) oxygen saturation ≤ 93% during air inhalation in resting state; 4) nasal flapping, three concave sign, stridor or wheezing; 5) disturbance of consciousness or convulsions; 6) food refusal or feeding difficulties, and dehydration signs. "Critical" was defined by the presence of any one of the following conditions: 1) respiratory failure requiring mechanical ventilation; 2) shock; 3) other organ failure that needed monitoring and treatment within the intensive care unit. The patients who met all of the following criteria after receiving treatment, were considered "cured": 1) temperature remained normal for at least 3 days; 2) improved respiratory symptoms; 3) two consecutive negative SARS-CoV-2 tests, taken > 24 hours apart.

Data collection and classification of sub-groups

Clinical data for both children and adult groups were recorded, including gender, age, presence of underlying diseases, clinical classifications and manifestations, treatments, and outcomes. Positive nucleic acid test duration was defined as the period between first positive nucleic acid result and the first negative nucleic acid result. Laboratory test measurements were also carried out, including routine blood test, liver and kidney functional measurements, interleukin-6, C-reactive protein, pro-calcitonin, erythrocyte sedimentation rate, etc. Chest computed tomography (CT) scans were used for imaging a nalyses.

The children and adult groups were divided into 3 age-based sub-groups. The sub-groups among the children were: "neonatal + infancy (0–1 years)", "early childhood + preschool (2–6 years)", and "school age + adolescence (7–18 years)". The sub-groups among the adults were: 19–40 years old, 41–60 years old, and ≥ 61 years old. The children and adult groups were also sub-divided into 3 sub-groups each, based on COVID-19 severity: mild, moderate, and severe + critical (Table 1).

Statistical analysis

All statistical analysis was performed using SPSS 26.0 (SPSS Inc., Chicago, IL, USA) and GraphPad Prism (version 8.0.2). Continuous variables were displayed as mean ± standard deviation (SD), while categorical variables were displayed as median (quartile). Significant differences between groups were determined using non-parametric one-way analysis of variance (ANOVA) and *t*-test for continuous variables, and χ^2 test for categorical variables. $p < 0.05$ (two-tailed) was considered statistically significant.

Results

This study identified 178 cases of Omicron COVID-19 in adults and 149 cases in children at the First Affiliated Hospital of Nanchang University between 7 December 2022 and 10 March 2023. Patient characteristics and clinical classifications among different sub-categories within the "children" and "adults" groups are presented in Table 1.

Among the children, ages ranged from 12 hours after birth to 14 years, with a median age of 1.0 (0.2, 6.0) year, while among the adults, the median age was 67.0 (54.0, 78.3) years. Furthermore, SARS-CoV-2

Table 1. Comparison of clinical classifications between different "children" and "adults" sub-groups; N (%).

"Children" sub-group	**Mild (n = 56)**	**Moderate (n = 32)**	**Severe + critical (n = 61)**	χ^2	***p value***
Age, N (%)					
Neonatal + infancy	32 (57.14)	20 (62.50)	19 (31.15)		
Early childhood + preschool	9 (16.07)	4 (12.50)	28 (45.90)	18.981	<0.001
School age + adolescence	15 (26.79)	8 (25.00)	14 (22.95)		
Gender, N (%)					
Male	29 (51.79)	19 (59.38)	31 (50.82)	2.117	0.347
Female	27 (48.21)	13 (40.62)	30 (49.18)		
Vaccination, N (%)					
Yes	19 (33.93)	9 (28.13)	26 (42.62)	1.264	0.532
No	37 (66.07)	23 (71.87)	35 (57.38)		
Pre-existing diseases, N (%)					
Yes	6 (10.71)	3 (9.38)	10 (16.39)	0.672	0.715
No	50 (89.29)	29 (90.62)	51 (83.61)		
"Adults" sub-group	**Mild (n = 7)**	Moderate **(n = 145)**	Severe + Critical **(n = 26)**	χ^2	***p value***
Age, N (%)					
19–40 years	1 (14.29)	4 (2.76)	2 (7.69)		
41–60 years	2 (28.57)	50 (34.48)	8 (30.77)	2.617	0.624
≥ 61 years	4 (57.14)	91 (62.76)	16 (61.54)		
Gender, N (%)					
Male	4 (57.14)	93 (64.14)	19 (73.08)	0.950	0.622
Female	3 (42.86)	52 (35.86)	7 (26.92)		
Vaccination, N (%)					
Yes	4 (57.14)	106 (73.10)	18 (69.23)	0.336	0.845
No	3 (42.86)	39 (26.90)	8 (30.77)		
Pre-existing diseases, N (%)					
Yes	5 (71.43)	98 (67.59)	19 (73.08)	0.983	0.612
No	2 (28.57)	47 (32.41)	7 (26.92)		

vaccination rates were 36.24% (54/149) in children, which was lower than for adults, at 71.91% (128/178; $\chi^2 = 41.810, p < 0.001$). A history of pre-existing disease was present in 19 (12.75%) children and 122 (68.5%) adults.

In terms of clinical outcomes, the only significant difference present was between different age sub-categories within the "children" group ($p < 0.05$). In particular, mild COVID-19 was most common among "neonatal + infancy", while severe + clinical was most

Table 2. Comparison of coronavirus disease 2019 (COVID-19) symptoms and treatments between "children" and "adults" groups (all N (%), except thermal spike, which is mean ± standard deviation).

Variable	**Children (n = 149)**	**Adults (n = 178)**	**T/χ^2**	***p value***
Symptoms, N (%)				
Fever	123 (82.55)	110 (61.80)	17.054	< 0.001
Cough	66 (44.30)	151 (84.83)	59.702	< 0.001
Expectoration	21 (14.09)	105 (58.99)	69.021	< 0.001
Chest tightness/shortness of breath	6 (4.03)	94 (52.81)	90.918	< 0.001
Panting/wheezing	13 (8.72)	5 (2.81)	5.457	0.019
Sore throat (hoarseness)	6 (4.03)	6 (3.37)	0.099	0.753
Tics and convulsion	33 (22.15)	0 (0.00)	43.848	< 0.001
Nasal congestion/runny nose	31 (20.81)	1 (0.56)	37.649	< 0.001
Nausea/vomiting	22 (14.77)	13 (7.30)	4.725	0.030
Chills	14 (9.40)	4 (2.25)	7.969	0.005
Fatigue	4 (2.68)	20 (11.24)	8.721	0.003
Headache	7 (4.70)	10 (5.62)	4.577	0.320
Abdominal pain/diarrhea	9 (6.04)	5 (2.81)	2.066	0.151
Myalgia/arthralgia	1 (0.67)	10 (5.62)	6.106	0.013
Thermal spike (°C)	39.01 ± 0.93	38.66 ± 0.65	3.394	0.001
Treatment, N (%)				
Polyethylene glycol interferon	64 (42.95)	3 (1.69)	84.786	< 0.001
Hormone	20 (13.42)	134 (75.28)	124.56	< 0.001
Antibiotics	126 (84.56)	172 (96.63)	14.609	< 0.001
Paxlovid	1 (0.67)	75 (42.13)	78.163	< 0.001
Azifudine	0 (0.00)	91 (51.12)	105.546	< 0.001
Pre-existing diseases, N (%)				
Yes	19 (12.75)	122 (68.54)	102.92	< 0.001
No	130 (87.25)	56 (31.46)		
Clinical classification, N (%)				
Mild	56 (37.58)	7 (3.93)	122.726	< 0.001
Moderate	32 (21.48)	145 (81.46)		
Severe + critical	61 (40.94)	26 (14.61)		

Table 3. Comparison of chest computed tomography (CT) imaging features N (%).

CT imaging features	Children (n = 81)	Adults (n = 173)	χ^2	*p value*
Abnormal image, N (%)	64 (79.01)	172 (99.42)	34.902	< 0.001
Ground-glass opacity, N (%)	4 (4.94)	52 (30.06)	20.255	< 0.001
Spots/patches, N (%)	40 (49.38)	115 (66.47)	6.776	0.009
Strip-like patterns, N (%)	8 (9.88)	43 (24.86)	7.714	0.005
Lung mini-nodules, N (%)	7 (8.64)	37 (21.39)	6.257	0.012

common among "early childhood + preschool" sub-categories, as shown in Table 1. Among the adults, no significant differences for clinical outcomes were present in any patient category, such as age, gender, vaccination history, or pre-existing diseases ($p > 0.05$; Table 1)

COVID-19 symptoms and treatments in "children" and "adults" groups

We examined the differences in COVID-19 symptoms between the children and adults and found that fever and its thermal spike, chills, occurrence of panting (wheezing), tics and convulsion, nasal congestion or runny nose, nausea, and vomiting were significantly higher among children, compared to adults ($p < 0.05$). On the other hand, among, coughing, expectoration, chest tightness or shortness of breath, fatigue, myalgia, arthralgia, were significantly more prevalent among adults than among children ($p < 0.05$). With respect to treatments, interferon therapy was significantly more common among children, while hormone, antibiotics, Paxlovid, and azifudine therapies were more prevalent among adults ($p < 0.05$) (Table 2).

Imaging changes in "children" and "adult " groups

Chest CT scans of adults had a significantly higher occurrence of pathological imaging features, such as abnormal images, ground-glass opacities, spots/patches, strip-like patterns, or lung mini-nodules, compared to those of children ($p < 0.05$; Table 3). This may suggest that these CT diagnostic landmarks for detecting COVID-19 may be less suitable for child patients, compared to adult patients, and that alternative approaches may be more accurate for diagnosing this disease in children.

Laboratory indices in "children" and "adults" groups

Laboratory marker indices between the two patient groups, such as the serum inflammation index, were compared to determine if any differences were present. Children had significantly increased white blood cell counts, and lymphocyte counts and percentages ($p < 0.05$). By contrast, the adults had increased neutrophil percentages and C-reactive protein levels ($p < 0.05$; Table 4).

Table 4. Comparison of serum inflammatory index markers between "children" and "adults" groups, N (%).

Serum inflammatory index marker	Children (n = 149)	Adults (n = 178)	χ^2	*p value*
High white blood cell count, N (%)	57/149 (38.26)	34/178 (19.10)	14.815	< 0.001
High lymphocyte count, N (%)	57/149 (38.26)	0/178 (0.00)	82.469	< 0.001
High lymphocyte percentage, N (%)	42/149 (28.19)	0/178 (0.00)	57.569	< 0.001
Low lymphocyte count, N (%)	24/149(16.11)	116/178(65.17)	79.737	< 0.001
Low lymphocyte percentage, N (%)	37/149(24.83)	125/178(70.22)	66.853	< 0.001
High neutrophil count, N (%)	36/149 (24.16)	51/178 (28.65)	0.838	0.360
High neutrophil percentage, N (%)	29/149 (19.46)	96/178 (53.93)	40.810	< 0.001
High C-reactive protein, N (%)	51/149 (34.23)	130/178 (73.03)	49.421	< 0.001
High pro-calcitonin, N (%)	86/92 (93.48)	90/101 (89.11)	1.144	0.285
High interleukin-6, N (%)	7/7 (100.00)	108/108 (100.00)	0.000	1.000
High erythrocyte sedimentation rate, N (%)	19/21 (90.48)	66/80 (82.50)	0.794	0.373

Table 5. Comparison of biochemical markers between "children" and "adults" groups (median [lower, upper quartiles]).

Biochemical Marker	Children (n = 149)	Adults (n = 178)	H	*p value*
Alanine transaminase (U/L)	20.30 (13.00, 31.94)	22.05 (16.00, 36.10)	3.362	0.067
Aspartate aminotransferase (U/L)	39.00 (30.00, 54.75)	26.95 (20.75, 36.73)	41.862	< 0.001
Alkaline phosphatase (U/L)	226.70 (178.90, 310.20)	74.35 (60.00, 91.10)	200.432	< 0.001
Creatinine (μmol/L)	29.09 (23.80, 39.40)	79.35 (63.05, 100.00)	188.657	< 0.001
Fasting blood glucose (mmol/L)	5.30 (4.87, 6.23)	7.13 (5.85, 9.30)	32.834	< 0.001
Lactate dehydrogenase (U/L)	328.20 (260.00, 402.40)	266.40 (222.10, 329.40)	23.615	< 0.001
Creatine kinase (U/L) K	120.00 (79.80, 176.90)	78.00 (42.00, 157.50)	19.585	< 0.001
Creatine kinase-MB (U/L)	29.00 (20.20, 41.90)	15.50 (11.90, 22.30)	69.562	< 0.001
D-dimer (mg/L)	0.76 (0.33, 1.39)	0.59 (0.31, 1.10)	9.225	0.002
Fibrinogen (g/L)	2.40 (1.99, 3.13)	4.47 (3.45, 5.07)	68.154	< 0.001

Table 6. Comparison of positive severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) nucleic acid durations between "children" and "adult" groups (median [25th, 75th percentiles]).

Clinical characteristics	Child (n = 149)	Adult (n = 178)	H	*p value*
Positive nucleic acid duration[a]	8.00 (6.00, 10.00)	12.00 (8.00, 16.00)	48.275	< 0.001
Vaccination				
Yes	8.00 (6.00, 10.25)	12.00 (8.00, 17.75)	20.613	< 0.001
No	9.00 (7.00, 14.00)	13.00 (9.00, 15.00)	23.999	< 0.001
Hazard ratio	9.389	0.254		
p value	0.002	0.614		
Clinical classification				
Mild	7.00 (6.00, 9.00)	8.00 (5.75, 14.00)	0.418	0.518
Moderate	8.50 (6.75, 12.00)	12.00 (8.00, 15.00)	9.025	0.003
Severe + critical	8.00 (7.00, 10.00)	14.00 (10.00, 22.00)	20.795	< 0.001
Hazard ratio	5.23	7.678		
p value	0.073	0.022		

[a]The criterion of positive nucleic acid duration was defined as the first positive nucleic acid result to the first negative nucleic acid result.

In the case of biochemical markers, the children had higher median aspartate aminotransferase, alkaline phosphatase, lactate dehydrogenase, creatinine kinase, creatine kinase-myocardial band and D-dimer levels; while the adults had higher median creatinine, fasting blood glucose, and fibrinogen levels ($p < 0.05$; Table 5).

Nucleic acid positive durations for the Omicron variant in "children" and "adult" groups

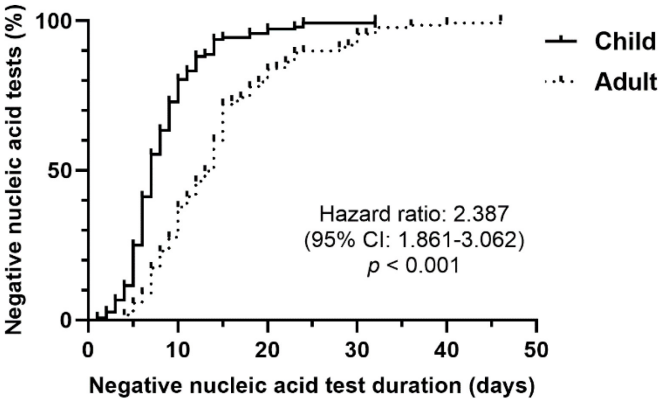
The overall duration of positive for nucleic acids tests was significantly longer in adults compared to children ($p < 0.05$); regardless of the vaccination status of the patients. However, vaccinated children had significantly shorter positive nucleic acid durations than unvaccinated children ($p < 0.05$). No such difference was noted between unvaccinated and vaccinated adults ($p < 0.05$). The durations of positive nucleic acid tests were also significantly longer for adults with "moderate" or "severe + critical" symptoms, compared to children with the same clinical classifications ($p < 0.05$). However, within the adults' group, significant differences in positive nucleic acid durations were present between the 3 clinical classifications ($p < 0.05$), with "mild" having the shortest, and "severe + clinical", the longest duration (Table 6).

The Kaplan-Meier curve was used to examine the cumulative negative conversion and improvement rates for Omicron variant nucleic acid between the two patient groups, and it was found that children had a higher cumulative negative conversion (Figure 1) and improvement rates (Figure 2), compared to adults; the differences were statistically significant ($p < 0.05$).

Discussion

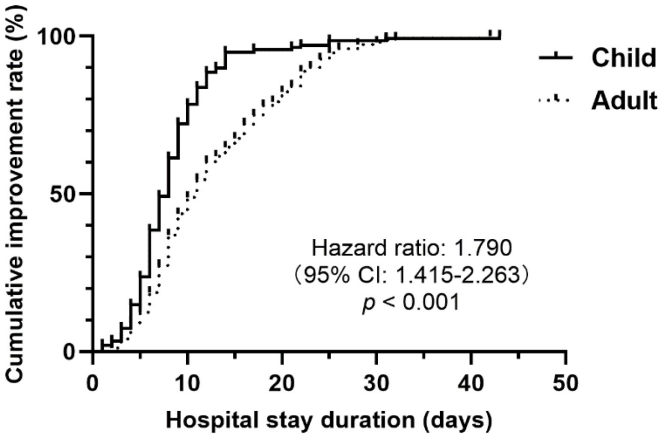
The Omicron variant is the most mutated strain of SARS-CoV-2, whose alterations in amino acid sequences, compared to prior SARS-CoV-2 strains, have been demonstrated to be widely distributed among several structural and non-structural viral proteins [8,9]. All of this alters the infectivity, immune escape capacities, and phenotypic characteristics of this

Figure 1. Cumulative negative conversion rate for SARS-CoV-2 nucleic acid among "children" and "adults" groups.



CI: confidence interval; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2.

Figure 2. Cumulative improvement rate for SARS-CoV-2 nucleic acid among "children" and "adults" groups.



CI: confidence interval; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2.

variant, rendering it with higher transmissibility, immune escape ability, and reinfection risk [6].

This study provided a comprehensive comparison of children and adult patient groups infected with the Omicron variant, with respect to clinical classifications, symptoms, imaging features, inflammation indices, biochemical markers, and positive nucleic acid test durations. We found that among children, "mild" and "severe + critical" were the most common clinical classifications, while among the adults, "moderate" was the most common. With respect to symptoms, fever was the most common among children, while it was coughing among adults. Other symptoms, including sputum production and those associated with upper respiratory tract infections, were similar to findings from previous studies [10,11]. Adults were also more frequently found with pathological imaging landmarks, such as ground-glass opacities, and had longer positive nucleic acid test durations.

The finding that "mild" COVID-19 was common among children was in line with observations by Zhang *et al*., who found that the majority of the 201 Omicron-infected children in their study were mild cases. However, unlike our study, no severe or critical cases were present in their study [12]. This may be due to our patient sample having greater numbers of children with fever or convulsion, resulting in a higher proportion of children being classified as having severe or critical cases. Furthermore, our study, was carried out after COVID-19 restrictions were lifted, resulting in increased hospitalization of more severe cases. Fever may have been the most common symptom among children due to greater activation of primary immune response and innate immune system pathways within the nasopharynx, compared to adults, leading to higher antiviral responses in the early stages of infection, as indicated by a study from Yale University [13]. Indeed, fever has been associated with increased immune responses, through higher body temperature which is able to promote lymphocyte migration and adhesion to infected draining lymph node, using T cell thermo-sensory pathways [14]. These higher temperatures also stimulate innate immunity processes, such as increasing cytotoxic activity, migration of natural killer cells to the inflammation site, and increasing granulocyte colony stimulating factor-induced bone marrow neutrophil release [15]. All of these phenomena serve as the likely underlying basis for more favorable clinical outcomes and CT imaging feature among the children, even though the proportion of severe/critical cases are higher than in adults.

Cough was the most common symptom among adults; possibly due to higher exposure to cigarette smoke and environmental pollution, compared to children, leading to weaker respiratory epithelial cells that are less able to resist SARS-CoV-2 infection. Furthermore, adult respiratory epithelial cells have higher expression levels of angiotensin-converting enzyme 2 (ACE2) on their cell surfaces [16], which is able to interact with the receptor-binding domain of the S1 subunit of the SARS-CoV-2 spike protein, thereby facilitating viral infection. By contrast, children have lower ACE2 expression levels within their nasal epithelium, which likely contributes to their lower susceptibility to infection, and predominance of "mild" disease classification [17]. ACE2 interactions also could serve as the underlying basis behind a number of other COVID-19 symptoms observed in our study, including fatigue, as it is also expressed on the surface of absorptive intestinal epithelial cells within the ileum and colon [18]. The possibility of SARS-CoV-2 being able to infect these cells is further supported by viral RNA being detected within fecal samples from infected patients. Therefore, we should focus on the breathlessness variable, and non-respiratory-related symptoms should be monitored as part of diagnosing patients infected with the Omicron variant.

With respect to lab test parameters, the total number of peripheral white blood cells was either at normal, or at increased levels, which also corresponded with decreased lymphocyte totals and percentages. This decrease was much greater among adults, compared to children, which was in line with the observations of Zhou *et al.* [19], where they found that among 104 patients with SARS-CoV-2, patients with lowered lymphocyte counts on the first day of admission were older than patients with normal counts. These lowered counts could also serve as an underlying basis for age ≥ 60 years old being a significant risk factor for SARS-CoV-2 infection, as reported in previous studies. Conversely, children having higher lymphocyte counts could be due to the aforementioned greater occurrence of fever, as well as anti-viral reactions, which promote immune responses [13,14]. Additional parameters, such as C-reactive protein, fibrinogen, D-dimer, liver and muscle enzymes, as well as ferritin, have been considered as major indicators for the immune response and prognosis of a patient. For instance, C-reactive protein levels rapidly increase when the human body is subjected to microbial invasion and tissue damage, thereby serving as a significant indicator of inflammatory and immune response, and subsequently, patient prognosis [20,21]. Similar associations with

patient prognoses have been found for fibrinogen and D-dimer, a product of fibrin degradation by fibrinolysin, all of whose levels have been found to be elevated among adult COVID-19 patients. More specifically, higher levels have been considered as markers of poor prognoses [22], thereby corresponding with observations made in this study that children had higher cumulative improvement rates for the Omicron variant, which is a marker of disease recovery. We also found, in line with previous studies, elevated levels of liver and muscle enzymes were present in some patients [23]. All of these alterations, particularly for C-reactive protein and D-dimer, were noted to be higher among adults, which could be due to viral invasion-induced inflammatory response and cytokine storms [24]. However, cytokine examination was not conducted to the same extent among children, compared to adults, and more significant confounding effects were present with the former group. Therefore, future studies should examine large sample sizes to fully determine differences in cytokine levels between children and adults.

Our study also found differences in treatments received between children and adult groups. For instance, interferon therapy was more common among children, while adults were more likely to receive oral antivirals, such as paxlovid and azifudine, or hormone therapies. This may be due to the lack of evidence for oral antivirals being effective in children, as previous clinical trials for such drugs, such as for nematavir/ritonavir, have only been carried out among adults. By contrast, interferon therapies, such as IFNα-1b and IFNα-2b have been demonstrated to be safe and effective treatments for pediatric viral pneumonia [25], which is one of the pathologies associated with SARS-CoV-2 infection. Additionally, antibiotics have been used to treat secondary bacterial infections, and glucocorticoids have often been administered for moderate-to-critical COVID-19 cases, which, however, require active serum glucose monitoring to minimize the occurrence of induced hyperglycemia [26]. The durations of positive nucleic acid tests were shorter among children compared to adults, and particularly among vaccinated individuals [27]. This may be due to vaccines aiding to neutralize SARS-CoV-2 spike proteins [6].

Limitations

Our study had some limitations. First, the study was a retrospective study with a relatively small sample size, and the conclusions need to be expanded for larger studies. Second, the changes in laboratory indexes before and after treatment were not compared. Furthermore, the clinical symptoms of the patients were not followed up after the negative nucleic acid tests.

Conclusions

Children infected with the Omicron mutant had increased innate immune system activity and lymphocyte numbers, resulting in more patients with milder clinical manifestations, lowered pro-inflammatory marker levels, and fewer pathological imaging landmarks. All of these contributed to them having faster post-infection recovery times, compared to adult patients. However, larger patient sample sizes should be examined in future studies to confirm these observations.

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