COMPARISON OF DIFFERENCES IN CLINICAL MANIFESTATIONS, LABORATORY FINDINGS AND OUTCOMES BETWEEN PEDIATRIC COVID-19 PATIENTS HOSPITALIZED DURING THE DELTA AND OMICRON PERIODS AT NARESUAN UNIVERSITY HOSPITAL, THAILAND

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Abstract. Little is known about the manifestations and outcomes of coronavirus disease-2019 (COVID-19) by viral variant type among children in Thailand. In this study we aimed to compare the clinical characteristics, laboratory findings and outcomes of pediatric COVID-19 patients during the 2 periods when the Delta and Omicron variants were predominating in order to inform efforts to control these infections in the study area. We conducted a retrospective review of the medical records of subjects aged <15 years admitted to Naresuan University Hospital, Thailand during 1 April 2021 - 30 November 2022 diagnosed with COVID-19 based on the results of a positive reverse transcriptase polymerase chain reaction (RT-PCR) test. Exclusion criteria for study subjects were not having a COVID-19 RT-PCR result in the chart or not being hospitalized. The minimum sample size calculated to be needed for the study was 390; 65 subjects who contracted COVID-19 when the delta variant predominated (Delta Group) and 325 who contracted COVID-19 when the omicron variant predominated (Omicron Group). A total of 396 subjects were included in the study, 68 (17.2%) in the Delta Group, 38 males (55.9%); and 328 (82.8%) in the Omicron Group, 175 males (53.4%). The median age of Delta Group subjects was 9 years and Omicron Group subjects was 6 years. Factors that were significantly different, respectively, between Delta Group and Omicron Group subjects were: anosmia (10.3% *vs* 0.3%) (p<0.001), a fever >38 °C (10.3% *vs* 34.2%) (p<0.001), sore throat (17.6% *vs* 35.7%) (p=0.004), diarrhea (4.4% *vs* 15.2%) (p=0.017), vomiting (4.4% *vs* 23.2%) (p<0.001), presence of lymphopenia (4.4% *vs* 21.9%) (p<0.001), C-reactive protein levels (0.6 mg/l *vs* 2.3 mg/l) (p<0.001) and procalcitonin levels (0.05 ng/ml *vs* 0.12 ng/ml) (p<0.001). The subjects in both groups had primarily mild disease, but there

was 1 death in the Omicron Group; none in the Delta Group. In summary, anosmia was more common in the Delta Group but high fever, sore throat, vomiting, diarrhea, gastrointestinal symptoms, lymphopenia and elevated inflammatory markers were more common in the Omicron Group. These findings show differences in the clinical presentations and laboratory results among pediatric patients by COVID-19 viral variant type. For the most part, subjects from both groups had mild symptoms except for 1 death in the Omicron Group. Further studies are needed to determine if these findings hold true for other institutions.

Keywords: COVID-19, SARS-CoV-2, Delta variant, Omicron variant, cycle threshold values

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INTRODUCTION

Coronavirus disease-2019 (COVID-19), caused by the severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2), has affected global health and economies worldwide. By 2023, there had been an estimated 771 million SARS-CoV-2 infections and nearly 7 million deaths from COVID-19 reported worldwide (WHO, 2023). Previous studies among adults (Ong *et al*, 2022; Cojocaru *et al*, 2022) showed patients with the Delta variant were more likely to be hospitalized and have more severe infections while the Omicron variant spread more rapidly but caused milder symptoms (Chatterjee *et al*, 2023).

Children usually have a mild course with COVID-19 (Dong *et al*, 2020; Laws *et al*, 2021). However, severe cases can occur, primarily among those with underlying health conditions or among infants aged <1 year (Tsankov *et al*, 2021; Harwood *et al*, 2022). During 2019-2021, SARS-CoV-2 mutated frequently, leading to changes in presentation and epidemiology (Jung *et al*, 2022). These changes have important implications for public health, such as the need for patient isolation and wearing masks and for development

of government policies and vaccines (Chatterjee *et al*, 2023).

In Thailand, there is little data about COVID-19 specifics among children aged <15 years (Satdhabudha *et al*, 2022; Shoji *et al*, 2022; Chaiyakulsil *et al*, 2022, Anugulruengkitt *et al*, 2021). However, previous studies have reported symptoms of COVID-19 among subjects aged <15 years are often mild or even non-existent and outcomes are generally good (Bai *et al*, 2021, Satdhabudha *et al*, 2022; Shoji *et al*, 2022). A study (Satdhabudha *et al*, 2022) conducted when the delta variant predominated (2021-2022), reported subjects had higher transmission rates but milder illness compared to the period prior to delta. With the change of the predominant variant from delta to omicron there is a need to evaluate the differences between these two variants among children in Thailand.

In this study we aimed to compare the clinical characteristics, laboratory findings and outcomes of pediatric COVID-19 patients during the 2 periods when the Delta and Omicron variants were predominating in order to inform efforts to control these infections in the study area.

MATERIALS AND METHODS

Study design and setting

We conducted a retrospective study at Naresuan University Hospital, a tertiary care hospital in northern Thailand among subjects aged <15 years with COVID-19 admitted to the pediatric isolation ward or field hospital of Naresuan University Hospital during 1 April 2021 - 30 November 2022.

Study subjects

Inclusion criteria for study subjects were being aged <15 years and being admitted to the study institutions during the study period with a diagnosis of COVID-19 confirmed by RT-PCR (using two gene targets, *N/E* and *ORF1ab*, with a Ct cutoff value of <40 as being positive and a cutoff value >40 as being negative). Exclusion criteria were being treated as an out-patient, not having a positive RT-PCR test for COVID-19 and having inadequate records. Subjects admitted during 1 April 2021 - 6 January 2022, the period when the COVID-19 delta variant predominated, according to Thai Ministry of Public Health (MoPH) nationwide surveillance data of random samples taken from patients at the study hospital, were placed in the Delta Group and

assumed to be infected with the delta variant. Subjects admitted during 7 January - 30 November 2022 when the omicron variant predominated, were placed in the Omicron Group and assumed to be infected with the omicron variant. Fever was defined as a temperature >37.5 °C. The severity of the COVID-19 infection in a subject was classified following World Health Organization (WHO) criteria (WHO, 2021) and ranged from asymptomatic to critical. Mild disease was defined as having mild symptoms without having pneumonia or hypoxia, moderate disease was defined as having pneumonia but no severe symptoms, severe disease was defined as having pneumonia and acute respiratory distress syndrome (ARDS), and critical disease was defined as being in a critical state and having ARDS and shock. Pneumonia was diagnosed based on symptoms, abnormal breath sounds, or having an infiltrate on a chest x-ray (WHO, 2021).

Data collection

During the study period when the delta variant predominated, the Thai Government required all subjects with COVID-19 to be hospitalized, but during the period when the omicron variant predominated, only those with moderate to severe symptoms were hospitalized. This results in a skewing of severity toward the omicron variant for which we could not account for in our study design and does affect our results.

The data collected from medical records were: subject demographics, signs and symptoms (fever, cough, rhinorrhea, sore throat, anosmia, dyspnea, chest pain, diarrhea, vomiting, headache, myalgia, rash, abdominal pain, eye symptom, seizure, desaturation), disease severity, final diagnosis, need for respiratory support and outcome. The laboratory data collected were: complete blood counts, liver function tests, inflammatory marker results, mean cycle threshold values for the RT-PCR tests and chest x-ray results.

Study size

The minimum sample size calculated to be needed for this study was 390 subjects: 65 in the Delta Group and 325 in the Omicron Group.

Statistical analysis

Categorical data are described as frequencies and percentages and were analyzed using Fisher's exact probability test. Normally

distributed continuous data are presented as means and standard deviations and were analyzed using the independent t-test. Non-normally distributed continuous data are presented as medians and interquartile ranges and were analyzed using the Mann-Whitney U test. We used an exploratory modeling strategy that included all risk factors for each strain. All risk factors in the model were prehospital risk factors and evaluated data were those obtained during the first two days of hospitalization.

We determined 95% two-sided confidence intervals for all factors. A p-value of < 0.05 was considered statistically significant. All statistical calculations were conducted using STATA, version 17 (Statacorp LLC, College Station, TX).

Ethical approval

This study was approved by the Institutional Review Board, Faculty of Medicine, Naresuan University Hospital (IRB No. P3-0081/2565). Written informed consent was not obtained from study subjects since the study was retrospective and no identifying data were used.

RESULTS

A total of 396 subjects were included in the study: 68 (17.2%) in the Delta Group and 328 (82.8%) in the Omicron Group. Of the total of 396 subjects, 213 (53.8%) were male (Table 1). The median age of subjects in the Delta Group was 9 years and in the Omicron Group was 6 years. The proportions of subjects in the Delta and Omicron Groups for those aged <1 year, 1-5 years, 5-10 years and 10-15 years were 2.9% and 12.2% (p=0.028), 30.9% and 37.2% (p=0.405), 38.2% and 24.7% (p=0.025) and 27.9% and 25.9% (p=0.763), respectively. A household contact was the source of infection for 62.9% of subjects (77.9% in the Delta Group and 59.8% in the Omicron group; p=0.006). The mean time between contact with a COVID-19 infected person and beginning to have symptoms of COVID-19 among subjects in the Delta Group was 4 days and in the Omicron Group was 2 days (p=0.002).

83.1% of subjects had no history of underlying disease; 16.9% had comorbidities: asthma/chronic lung/allergic disease in 3.5%. There was no significant difference in history of comorbidities between the Delta and Omicron Groups. 26.8% of subjects had a history of COVID-19 vaccination. Fewer subjects in the Delta Group had been vaccinated (7.4%) than the Omicron

Table 1

Characteristics of study subjects

Characteristic	Total (N = 396)	Variant groups		*p*-value
		Delta (N = 68)	Omicron (N = 328)	
Sex, *n* (%)				0.790
Female	183 (46.2)	30 (44.1)	153 (46.6)	
Male	213 (53.8)	38 (55.9)	175 (53.4)	
Age, median (IQR)	6 (2, 11)	8.5 (5, 11)	6 (2, 11)	0.023
Age group, *n* (%)				
<1 year	42 (10.6)	2 (2.9)	40 (12.2)	0.028
1 to <5 years	143 (36.1)	21 (30.9)	122 (37.2)	0.405
5 to <10 years	107 (27.0)	26 (38.2)	81 (24.7)	0.025
10-15 years	104 (26.3)	19 (27.9)	85 (25.9)	0.763
Nutritional status[a,b], *n* (%)				0.194
Normal	328 (83.0)	54 (80.6)	274 (83.5)	0.479
Failure to thrive	23 (5.8)	7 (10.4)	16 (4.9)	0.091
Obesity	44 (11.2)	6 (9.0)	38 (11.6)	0.672
Body mass index (kg/m^2), median (IQR)	17.5 (15, 21)	16.9 (15, 20)	17.6 (15, 21)	0.538

Table 1 (cont)

Characteristic	Total (N = 396)	Variant groups		*p*-value
		Delta (N = 68)	Omicron (N = 328)	
Sources of exposure to COVID-19, *n* (%)				0.015
Unknown	48 (12.1)	3 (4.4)	45 (13.7)	0.039
Household	249 (62.9)	53 (77.9)	196 (59.8)	0.006
School	72 (18.2)	11 (16.2)	61 (18.6)	0.731
Family's workplace		5 (1.3)	1 (1.5)	4 (1.2)
Neighborhood	21 (5.3)	0 (0)	21 (6.4)	0.033
Social gatherings	1 (0.3)	0 (0)	1 (0.3)	0.828
Day of contact, median (IQR)	2 (1, 4)	4 (2, 5)	2 (1, 4)	0.002
Underlying disease, *n* (%)				0.733
No underlying disease	329 (83.1)	58 (85.3)	271 (82.6)	
With underlying diseases	67 (16.9)	10 (14.7)	57 (17.4)	
Asthma/Chronic lung disease	14 (3.5)	1 (1.5)	13 (4.0)	
Allergy	14 (3.5)	3 (4.4)	11 (3.4)	
Neurologic diseases	9 (2.3)	0 (0)	9 (2.7)	
Hematologic disorders	8 (2.0)	2 (3.0)	6 (1.8)	

Table 1 (cont)

Characteristic	Total (N = 396)	Variant groups		*p*-value
		Delta (N = 68)	Omicron (N = 328)	
Cardiac disease	6 (1.5)	2 (3.0)	4 (1.2)	
Delayed development	4 (1.0)	1 (1.5)	3 (0.9)	
Diabetes Mellitus/endocrine	4 (1.0)	0 (0)	4 (1.2)	
Malignancy	3 (0.8)	0 (0)	3 (0.9)	
Others	5 (1.3)	1 (1.5)	4 (1.2)	
COVID-19 vaccination status, *n* (%)				
Unvaccinated	285 (72.0)	61 (89.7)	224 (68.3)	<0.001
Vaccinated	106 (26.8)	5 (7.4)	101 (30.8)	<0.001
Unknown	5 (1.3)	2 (2.9)	3 (0.9)	0.205

[a]Nutritional status is defined as follow - Failure to thrive: weight consistently below the 3rd percentile for age and sex; obesity: weight-for-length/height or BMI-for-age is greater than 3 standard deviations (SD) above the WHO growth standard median for the age at birth to 5 years and is greater than 2 standard deviations above the WHO Growth Reference median for children aged 5-15 years; otherwise, the nutritional status is normal (WHO, 2017).

[b]Calculations of percentages for Total and Delta columns were based on $N = 395$ and $N = 67$, respectively because there was no record of body weight and height of one patient.

COVID-19: coronavirus disease 2019; IQR: interquartile range; kg/m2: kilogram per square meter

Group (30.8%) (7.4% *vs* 30.8%, $p<0.001$) (Table 1). This makes sense since vaccines approved for use in children did not appear until later in the study.

The most common symptoms among subjects were fever (n = 285, 72.0%), cough (n = 241, 60.9%), rhinorrhea (n = 132, 33.3%) and sore throat (n = 129, 32.6%). Significantly more subjects in the Delta Group than the Omicron Group had anosmia (10.3% *vs* 0.3%, $p<0.001$), rash (8.8% *vs* 2.7%, $p=0.029$), temperature >38°C (34.2% *vs* 10.3%, $p<0.001$), sore throat (35.7% *vs* 17.6 %, $p=0.004$), diarrhea (15.2% *vs* 4.4%, $p=0.017$) and vomiting (23.2% *vs* 4.4%, $p<0.001$) (Table 2).

Significantly fewer subjects in the Delta Group than the Omicron Group had pharyngitis (4.4% *vs* 30.8%, $p<0.001$), gastroenteritis (4.4 % *vs* 17.1%, $p=0.017$), croup (0% *vs* 0.9%, $p=0.567$) and febrile seizures (0% *vs* 2.4%, $p=0.361$) (Table 2).

2.9% of subjects in the Delta Group and 3.3% of subjects in the Omicron Group needed respiratory support. One subject with cerebral palsy and developmental delay died due to severe pneumonia, ARDS and multiple organ failure in the Omicron Group. None of the subjects in the Delta Group died.

Laboratory results were available for 394 of the 396 subjects (99.4%). The proportions of subjects with lymphopenia in the Delta and Omicron Groups were 4.4% and 21.9% ($p<0.001$), respectively. The platelet counts among the subjects in the Delta and Omicron Groups were 303,000 cells/mm^3 and 272,000 cells/mm^3 ($p<0.001$), respectively. The absolute neutrophil counts among subjects in the Delta and Omicron Groups were 3,117.5 cells/mm^3 and 3,387.2 cells/mm^3 ($p=0.027$), respectively. The mean C-reactive protein levels among subjects in the Delta and Omicron groups were 0.6 mg/l and 2.3 mg/l ($p<0.001$), respectively. The mean procalcitonin levels among subjects in the Delta and Omicron Groups were 0.05 ng/ml and 0.12 ng/ml ($p<0.001$) (Table 3).

Pneumonia was found on chest radiography among 93 subjects (23.5%). The most common abnormal finding seen on chest radiography was a ground-glass opacity, which was found in 27.9% of subjects in the Delta Group and 11.6% of subjects in the Omicron Group ($p=0.001$) (Table 3).

The mean (±standard deviation (SD)) RT-PCR cycle threshold (Ct) values for the nucleocapsid/envelope

Table 2

Clinical characteristics of study subjects

Characteristics	Total (N = 396)	Dominant variant group		*p*-value
		Delta (N = 68)	Omicron (N = 328)	
Onset of symptom, median (IQR)	2 (1, 3)	2 (1, 4)	1 (1, 3)	0.069
Clinical manifestations, *n* (%)				
Asymptomatic	28 (7.1)	13 (19.1)	15 (4.6)	<0.001
Fever	285 (72.0)	33 (48.5)	252 (76.8)	<0.001
Body temperature >38°C	119 (30.0)	7 (10.3)	112 (34.2)	<0.001
Fever (°C), median (range),	37 (36.0-41.0)	36.7 (36.0-39.0)	37 (36.0-41.0)	<0.001
Fever duration, median (range), day	2 (1-3)	2 (1-4.5)	1 (1-3)	0.058
Cough	241 (60.9)	38 (55.9)	203 (61.9)	0.413
Rhinorrhea	132 (33.3)	22 (32.4)	110 (33.5)	0.889
Sore throat	129 (32.6)	12 (17.6)	117 (35.7)	0.004
Anosmia	8 (2.0)	7 (10.3)	1 (0.3)	<0.001
Dyspnea	25 (6.3)	1 (1.5)	24 (7.3)	0.097
Chest pain	3 (0.8)	0 (0)	3 (0.9)	0.567
Diarrhea	53 (13.4)	3 (4.4)	50 (15.2)	0.017
Vomiting	79 (19.9)	3 (4.4)	76 (23.2)	<0.001
Headache	36 (9.1)	7 (10.3)	29 (8.8)	0.648
Myalgia/arthralgia	8 (2.0)	1 (1.5)	7 (2.1)	0.588
Rash	15 (3.8)	6 (8.8)	9 (2.7)	0.029

Table 2 (cont)

Characteristics	Total (N = 396)	Dominant variant group		*p*-value
		Delta (N = 68)	Omicron (N = 328)	
Clinical manifestation, *n* (%) (continue)				
Abdominal pain	3 (0.8)	0 (0)	3 (0.9)	0.172
Eye symptom	3 (0.8)	0 (0)	3 (0.9)	0.567
Seizure	8 (2.0)	0 (0)	8 (2.4)	0.361
Desaturation	5 (1.3)	1 (1.5)	4 (1.2)	0.612
Disease severity[a], *n* (%)				
Asymptomatic	26 (6.5)	14 (20.6)	12 (3.7)	<0.001
Mild	239 (60.4)	29 (42.6)	210 (64.0)	0.002
Moderate	124 (31.3)	23 (33.8)	101 (30.8)	0.667
Severe	6 (1.5)	2 (3.0)	4 (1.2)	0.275
Critically ill	1 (0.3)	0 (0)	1 (0.3)	0.828
Clinical manifestations, *n* (%)				
Asymptomatic	26 (6.5)	14 (20.6)	12 (3.7)	<0.001
Acute febrile illness	18 (4.5)	3 (4.4)	15 (4.6)	0.626
Upper respiratory tract infection	70 (17.6)	21 (30.9)	49 (14.9)	0.003
Acute pharyngitis	104 (26.3)	3 (4.4)	101 (30.8)	<0.001
Acute bronchitis	9 (2.3)	1 (1.5)	8 (2.4)	0.524
Acute gastroenteritis/gastritis	59 (14.9)	3 (4.4)	56 (17.1)	0.017

Table 2 (cont)

Characteristics	Total (N = 396)	Dominant variant group		*p*-value
		Delta (N = 68)	Omicron (N = 328)	
Pneumonia	97 (24.5)	23 (33.8)	74 (22.6)	0.062
Croup	3 (0.8)	0 (0)	3 (0.9)	0.567
Febrile seizure	8 (2.0)	0 (0)	8 (2.4)	0.361
Diabetic ketoacidosis	1 (0.3)	0 (0)	1 (0.3)	0.828
Acute respiratory distress syndrome with multiple organ failure	1 (0.3)	0 (0)	1 (0.3)	0.828
Respiratory support, *n* (%)				
None	383 (96.6)	66 (97.1)	317 (96.7)	0.608
Cannula	11 (2.8)	2 (2.9)	9 (2.7)	0.590
HHHFNC	1 (0.3)	0 (0)	1 (0.3)	0.828
ET-tube	1 (0.3)	0 (0)	1 (0.3)	0.828
Outcomes, *n* (%)				
Recovered	332 (83.8)	62 (91.2)	270 (83.3)	0.255
Improved	63 (15.9)	6 (8.8)	57 (17.4)	0.052
Deceased	1 (0.3)	0 (0)	1 (0.3)	0.828

[a]Mild: symptoms without pneumonia or hypoxia; Moderate: pneumonia without severe symptoms; Severe: pneumonia with acute respiratory distress syndrome (ARDS); Critical: ARDS or septic shock; otherwise, it is asymptomatic

COVID-19: coronavirus disease 2019, ET-tube: endotracheal tube; HHHFNC: humidified high flow nasal cannular; IQR: interquartile range

Table 3

Laboratory findings among study subjects

Laboratory result	Total (N = 396)	Dominant variant group		*p*-value
		Delta (N = 68)	Omicron (N = 328)	
Complete blood count (CBC)				
WBC (cells/mm^3), median (IQR)	6785 (5310, 8650)	6600 (5440, 8215)	6820 (5300, 8720)	0.577
ANC (cells/mm^3), median (IQR)	3338.5 (2229.1, 4851)	3117.5 (1865.9, 4013.7)	3387.2 (2297.6, 5124.7)	0.027
% PMN (cells/mm^3), median (IQR)	51.1 (36.4, 64.5)	45.95 (33.8, 53.2)	52.65 (37.6, 68.7)	<0.001
% Lymphocyte (cells/mm^3), median (IQR)	39.4 (25.8, 53.8)	43.3 (36.9, 57.35)	37.1 (21.6, 53.1)	<0.001
ALC (cells/mm^3), median (IQR)	2494.1 (1550.8, 3582)	2930.9 (2294.4, 3851.9)	2310.8 (1390.9, 3447.6)	<0.001
Platelet count (cells/mm^3), median (IQR)	278,500 (227,000, 334,000)	303,000 (275,000, 379,000)	272,000 (218,000, 326,000)	<0.001
Lymphopenia (<1500 cells/mm^3), *n* (%)	94 (23.9)	3 (4.4)	91 (21.9)	<0.001
Neutropenia (<1500 cells/mm^3), *n* (%)	44 (11.2)	10 (14.7)	34 (10.4)	0.293
Thrombocytopenia (<150,000 cells/mm^3), *n* (%)	8 (2.03)	0 (0)	8 (2.5)	0.361

Table 3 (cont)

Laboratory result	Total (N = 396)	Dominant variant group		*p*-value
		Delta (N = 68)	Omicron (N = 328)	
Liver function test				
AST (U/l), mean ± SD	36.8 ±18.4	33.7 ± 17.5	37.4 ± 18.5	0.164
ALT (U/l), mean ± SD	21.7 ±18.9	18.9 ± 14.4	22.2 ± 19.7	0.233
Inflammatory markers				
C-reactive protein (mg/l), median (IQR)	1.9 (0.6, 5.6)	0.6 (0.6, 2.2)	2.3 (0.7, 6.4)	<0.001
Procalcitonin(ng/ml), median (IQR)	0.10 (0.05, 0.23)	0.05 (0.03, 0.08)	0.12 (0.06, 0.26)	<0.001
D-dimer (ng/ml), mean ± SD	1398.6 ± 210.9	1124.5 ± 522.0	1444.6 ± 203.5	0.595
LDH (U/l), mean (± SD)	247.6 ± 63.7	254.4 ± 61.8	246.5 ± 64.0	0.425
Ferritin (ng/ml), mean (± SD)	148.9 ± 21.1	113.5 ± 16.4	153.6 ± 23.8	0.541
RT-PCR results (Ct values), mean ± SD				
N/E gene	19.0 ± 5.7	23.7 ± 8.4	18.0 ± 4.4	<0.001
ORF1ab gene	21.2 ± 5.4	25.8 ± 7.7	20.2 ± 4.3	<0.001

Table 3 (cont)

Laboratory result	Total (N = 396)	Dominant variant group		*p*-value
		Delta (N = 68)	Omicron (N = 328)	
Chest X-ray[a], *n* (%)				0.014
Normal	302 (76.5)	43 (63.2)	259 (79.2)	0.008
Ground glass opacity	57 (14.4)	19 (27.9)	38 (11.6)	0.001
Patchy opacity	13 (3.3)	3 (4.4)	10 (3.1)	0.474
Perihilar	11 (2.8)	1 (1.5)	10 (3.1)	0.698
Consolidation	5 (1.3)	0 (0)	5 (1.5)	0.593
Interstitial	4 (1.0)	2 (3.0)	2 (0.6)	0.138
Perihilar with ground glass opacity	2 (0.5)	0 (0)	2 (0.6)	0.686
Perihilar with patchy opacity	1 (0.2)	0 (0)	1 (0.3)	0.828

[a]Calculations of percentages for Total and Omicron columns were based on N = 395 and N = 327, respectively because one patient did not perform chest X-ray.

COVID-19: coronavirus disease 2019, ALT: Alanine aminotransferase; ALC: absolute lymphocyte count; ANC: absolute neutrophil count; AST: Aspartate transaminase; Ct values: cycle threshold values; IQR: interquartile range; LDH: lactate dehydrogenase; mg/l: milligram per liter; ng/ml: nanogram per milliliter; *N/E* gene: nucleocapsid/envelope gene; *ORF1ab* gene: open reading frame of 1ab gene; PMN: polymorphonuclear; RT-PCR: reverse transcriptase polymerase chain reaction; SD: standard deviation; U/l: unit per liter; WBC: white blood count

(N/E) genes in the Delta and Omicron Groups were 23.7 (±8.4) and 18.0 (±4.4) (p<0.001), respectively. The mean (±SD) RT-PCR cycle threshold (Ct) values for the open reading frame of the *1ab (ORF1ab)* genes in the Delta and Omicron Groups were 25.8 (±7.7) and 20.2 (±4.3) (p<0.001), respectively.

DISCUSSION

In our study, subjects in the Omicron Group were significantly younger than subjects in the Delta group, similar to the findings in studies from Pakistan, Korea, and the USA (Abbas *et al*, 2023; Han *et al*, 2023; Quintero *et al*, 2022). This age discrepancy may be attributable to two factors: (1) the increased transmissibility of the Omicron variant compared to the Delta variant (CDC COVID-19 Response Team, 2021), and (2) the relaxed quarantine policies during the Omicron period, which may have led to a higher proportion of infections among younger individuals.

Fever and cough were the most common symptoms among subjects in both the Delta and Omicron Groups, similar to previous studies (de Souza *et al*, 2020; Li *et al*, 2022; Sumner *et al*, 2023). However, a study from China reported fever was the most common symptom of COVID-19 among subjects, followed by cough (Cui *et al*, 2021). In our study, the incidences of fever, sore throat, vomiting, diarrhea, croup and febrile seizures were significantly more common among subjects in the Omicron than the Delta Group. A study from Spain reported fever and diarrhea were significantly more common among subjects with omicron compared to prior COVID-19 variants (Tagarro *et al*, 2022b). A study from Malaysia reported croup and febrile seizures were significantly more common among subjects with omicron than delta variants (Ng *et al*, 2024).

In our study, anosmia was significantly less common among subjects in the Omicron than the Delta Group. A previous study from Mexico also reported anosmia was significantly less common among subjects with the omicron variant than other variants (Peña Rodríguez *et al*, 2023).

In our study, lymphopenia was significantly more common among subjects in the Omicron than the Delta Group, in contrast to studies from China and Brazil who reported lymphopenia was significantly less common among subjects with the omicron than the delta variant (Cui *et al*, 2021; Cui *et al*, 2020; de Souza *et al*, 2020). In our study, the mean

C-reactive protein and procalcitonin levels were significantly higher among subjects in the Omicron than the Delta Group, similar to the findings of a study from Turkey (Guner Ozenen *et al*, 2021).

Among our study subjects, an abnormal chest x-ray was found in 23.5% of subjects, with ground-glass opacities, patchy infiltrates and lung consolidations being the most common abnormal findings. A study from China reported abnormal chest x-ray results in 59% of subjects, with the most common abnormal findings being ground-glass opacities and patchy infiltrates (Cui *et al*, 2021).

In our study, the mean Ct values of both viral genes were significantly lower in the Omicron Group than in the Delta Group, indicating a higher transmissibility of the Omicron variant (Hay *et al*, 2021; Setiabudi *et al*, 2022). Previous studies have reported conflicting results, with a study from Qatar (Butt *et al*, 2022) showing lower Ct results among omicron than other variants but a study from Brazil (Franco-Miraglia *et al*, 2023) showing lower Ct results among gamma and delta than omicron variants.

In our study, most subjects had mild symptoms. We did have one fatality in the Omicron Group (0.25%) who had underlying cerebral palsy and developmental delay. Previous studies from Thailand, China, Spain and Malaysia have reported COVID-19 mortality rates among children in the range of 0-0.45% (Chaiyakulsil *et al*, 2022; Cui *et al*, 2021; Tagarro *et al*, 2022a; Ng *et al*, 2024).

Our sample size was not sufficient to adequately compare mortality rates between omicron and delta variants but a previous study from Qatar and the USA reported lower mortality rates among omicron than delta variant infected subjects (Butt *et al*, 2022; Bahl *et al*, 2023). Higher mortality rates have been reported among subjects with underlying immunosuppression, such as cancer and prematurity (Chaiyakulsil *et al*, 2022; Cui *et al*, 2021; Tagarro *et al*, 2022a). A study from Korea (Choi *et al*, 2023) reported subjects with COVID-19 and underlying cerebral disease were more likely to have severe COVID-19, as was seen in our study where the only death was in a case with underlying cerebral palsy. A previous study reported COVID-19 patients from low and middle-income countries had significantly higher mortality rates than subjects from high-income countries (Kitano *et al*, 2021).

Our study had some limitations.

First, the SARS-CoV-2 strain in each patient was not confirmed. Instead, we relied on variant surveillance data from our hospital and Thailand's Ministry of Public Health. Second, due to a government policy shift in Thailand, which mandated hospitalization for all COVID-19 patients during the early Delta period but not in the Omicron period, a comparison of the severity of infection among hospitalized patients cannot be made. Lastly, the generalizability of our findings may be limited due to the single-center design and the small sample size, particularly regarding patients with severe or critical illnesses. This limited sample size restricts our ability to definitively assess the relationship between disease severity and Ct values.

In summary, this study showed that more subjects with COVID-19 admitted during the omicron period presented with high fever, gastrointestinal symptoms, lymphopenia, elevated inflammatory markers and lower Ct values than those hospitalized during the Delta period. Despite the observed clinical differences, both periods were characterized by predominantly mild disease and favorable clinical outcomes. We conclude our findings highlight variations in the clinical presentation of pediatric patients with COVID-19 during different periods, but the severity of symptoms in both groups was mild. Only one death occurred and that was in the Omicron Group. Further studies are needed determining the SAR-CoV-2 variant, with a larger sample size and at multiple centers.

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CONFLICT OF INTEREST DISCLOSURE

None of the authors declared a conflict of interest.

REFERENCES

Abbas Q, Khalid F, Shahbaz FF, *et al*. Clinical and epidemiological features of pediatric population hospitalized with COVID-19: a multicenter longitudinal study (March 2020-December 2021) from Pakistan. *Lancet Reg Health Southeast Asia* 2023; 11: 100176.

Anugulruengkitt S, Teeraananchai S, Chantasrisawad N, Promsena P, Jantarabenjakul W, Puthanakit T. Clinical outcomes of pediatric COVID-19 in a tertiary care center in Bangkok, Thailand. *IJID Reg* 2021; 1: 159-62.

Bahl A, Mielke N, Johnson S, Desai A, Qu L. Severe COVID-19 outcomes in pediatrics: An observational cohort analysis comparing Alpha, Delta, and Omicron variants. *Lancet Reg Health Am* 2023; 18: 100405.

Bai Y, Gao L, Wang X, *et al*. Epidemiological characteristics and clinical manifestations of pediatric patients with COVID-19 in China: A multicenter retrospective study. *Pediatr Investig* 2021;5(3):203-210.

Butt AA, Dargham SR, Loka S, *et al*. Coronavirus disease 2019 disease severity in subjects infected with the Omicron variant. *Clin Infect Dis* 2022; 75(1): e361-7.

Centers for Disease Control and Prevention Coronavirus Disease 2019 Response Team (CDC COVID-19 Response Team). SARS-CoV-2 B.1.1.529 (Omicron) variant - United States, December 1-8, 2021. *MMWR Morb Mortal Wkly Rep* 2021; 70(50):1731-4.

Chaiyakulsil C, Sritipsukho P, Satdhabudha A, *et al*. An epidemiological study of pediatric COVID-19 in the era of the variant of concern. *PLoS One* 2022; 17(4): e0267035.

Chatterjee S, Bhattacharya M, Nag S, Dhama K, Chakraborty C. A detailed overview of SARS-CoV-2 Omicron: its sub-variants, mutations and pathophysiology, clinical characteristics, immunological landscape, immune escape, and therapies. *Viruses* 2023; 15(1): 167.

Choi SH, Choi JH, Lee JK, *et al*. Clinical characteristics and outcomes of subjects with SARS-CoV-2 infection during the Delta and Omicron variant-dominant periods in Korea. *J Korean Med Sci* 2023; 38(9): e65.

Cojocaru C, Cojocaru E, Turcanu AM, Zaharia DC. Clinical challenges of SARS-CoV-2 variants (Review). *Exp Ther Med* 2022; 23(6): 416.

Cui X, Zhang T, Zheng J, *et al*. Subjects with coronavirus disease 2019: a review of demographic, clinical, laboratory, and imaging features in pediatric patients. *J Med Virol* 2020; 92(9): 1501-10.

Cui X, Zhao Z, Zhang T, *et al*. A systematic review and meta-analysis of subjects with coronavirus disease

2019 (COVID-19). *J Med Virol* 2021; 93(2): 1057-69.

de Souza TH, Nadal JA, Nogueira RJN, Pereira RM, Brandão MB. Clinical manifestations of subjects with COVID-19: a systematic review. *Pediatr Pulmonol* 2020; 55(8): 1892-9.

Dong Y, Mo X, Hu Y, *et al*. Epidemiology of COVID-19 among subjects in China. *Pediatrics* 2020; 145(6): e20200702.

Franco-Miraglia F, Martins-Freitas B, Doi AM, Santana RAF, Pinho JRR, Avelino-Silva VI. Associations of SARS-CoV-2 cycle threshold values with age, gender, sample collection setting, and pandemic period. *Rev Inst Med Trop Sao Paulo* 2023; 65: e53.

Guner Ozenen G, Sahbudak Bal Z, Umit Z, *et al*. Demographic, clinical, and laboratory features of COVID-19 in subjects: the role of mean platelet volume in predicting hospitalization and severity. *J Med Virol* 2021; 93(5): 3227-37.

Han MS, Kim KM, Oh KJ, *et al*. Distinct clinical and laboratory features of COVID-19 in subjects during the Pre-Delta, Delta and Omicron wave. *Pediatr Infect Dis J* 2023; 42(5): 423-8.

Harwood R, Yan H, Talawila Da Camara N, *et al*. Which children and young people are at higher risk of severe disease and death after hospitalisation with SARS-CoV-2 infection in children and young people: a systematic review and individual patient meta-analysis. *EClinicalMedicine* 2022; 44: 101287.

Hay JA, Kennedy-Shaffer L, Kanjilal S, *et al*. Estimating epidemiologic dynamics from cross-sectional viral load distributions. *Science* 2021; 373(6552): eabh0635.

Jung C, Kmiec D, Koepke L, *et al*. Omicron: what makes the latest SARS-CoV-2 variant of concern so concerning? *J Virol* 2022; 96(6): e0207721.

Kitano T, Kitano M, Krueger C, *et al*. The differential impact of pediatric COVID-19 between high-income countries and low- and middle-income countries: a systematic review of fatality and ICU admission in children worldwide. *PLoS One* 2021; 16(1): e0246326.

Laws RL, Chancey RJ, Rabold EM, *et al*. Symptoms and transmission of SARS-CoV-2 among subjects — Utah and Wisconsin, March-May 2020. *Pediatrics* 2021; 147(1): e2020027268.

Li YC, Ma Z, Zhong HY, You HL. Clinical characteristics of subjects with omicron SARS-CoV-2 infection in Changchun, China from March to April 2022: a retrospective study. *Front Pediatr* 2022; 10: 990944.

Ng DC, Liew CH, Tan KK, *et al*. Clinical severity of Omicron and Delta SARS-CoV-2 infections in children.

Pediatr Int 2024; 66(1): e15777.

Ong SWX, Chiew CJ, Ang LW, *et al*. Clinical and virological features of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants of concern: a retrospective cohort study comparing B.1.1.7 (Alpha), B.1.351 (Beta), and B.1.617.2 (Delta). *Clin Infect Dis* 2022; 75(1): e1128-36.

Peña Rodríguez M, Hernández Bello J, Vega Magaña N, *et al*. Prevalence of symptoms, comorbidities, and reinfections in individuals infected with wild-type SARS-CoV-2, Delta, or Omicron variants: a comparative study in western Mexico. *Front Public Health* 2023; 11: 1149795.

Quintero A, Eisner M, Sayegh R, *et al*. Differences in SARS-CoV-2 clinical manifestations and disease severity in children and adolescents by infecting variant. *Emerg Infect Dis* 2022; 28(11): 2270-80.

Satdhabudha A, Chaiyakulsil C, Sritipsukho P, *et al*. Epidemiological and clinical characteristics of pediatric COVID-19 in the Tertiary care system in Thailand: comparative Delta and Pre-Delta era. *Mediterr J Hematol Infect Dis* 2022; 14(1): e2022044.

Setiabudi D, Sribudiani Y, Hermawan K, Andriyoko B, Nataprawira HM. The Omicron variant of concern: the genomics, diagnostics, and clinical characteristics in children. *Front Pediatr* 2022; 10: 898463.

Shoji K, Akiyama T, Tsuzuki S, *et al*. Comparison of the clinical characteristics and outcomes of COVID-19 in subjects before and after the emergence of Delta variant of concern in Japan. *J Infect Chemother* 2022; 28(4): 591-4.

Sumner MW, Xie J, Zemek R, *et al*. Comparison of symptoms associated with SARS-CoV-2 variants among subjects in Canada. *JAMA Netw Open* 2023; 6(3): e232328.

Tagarro A, Cobos-Carrascosa E, Villaverde S, *et al*. Clinical spectrum of COVID-19 and risk factors associated with severity in Spanish subjects. *Eur J Pediatr* 2022a; 181(3): 1105-15.

Tagarro A, Coya ON, Pérez-Villena A, *et al*. Features of COVID-19 in children during the Omicron wave compared with previous waves in Madrid, Spain. *Ped Infect Dis J* 2022b; 41: e249-51.

Tsankov BK, Allaire JM, Irvine MA, *et al*. Severe COVID-19 infection and pediatric comorbidities: a systematic review and meta-analysis. *Int J Infect Dis* 2021; 103: 246-56.

World Health Organization (WHO). Guideline: Assessing and managing subjects at primary health-care facilities to prevent overweight and obesity in the context of the double burden of malnutrition: updates

for the integrated management of childhood illness (IMCI), 2017 [cited 2023 Feb 19]. Available from: URL: https://www.ncbi.nlm.nih.gov/books/n/who259133/pdf/

World Health Organization (WHO). Living guidance for clinical management of COVID-19, 2021 [cited 2023 Nov 01]: Available from: URL: https://iris.who.int/bitstream/handle/10665/349321/WHO-2019-nCoV-clinical-2021.2-eng.pdf?sequence=1

World Health Organization (WHO). COVID-19 epidemiological update: Edition 160 published 27 October 2023, 2023 [cited 2023 Nov 01]. Available from: URL: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20231027_covid-19_epi_update_160.pdf?sfvrsn=35a4f550_3&download=true