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Original Article

Epidemiological and Clinical Characteristics of Pediatric COVID-19 in the Tertiary Care System in Thailand: Comparative Delta and pre-Delta Era

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Abstract. ***Background*: Few studies had focused on the epidemiological and clinical characteristics of pediatric COVID-19 (SARS-CoV-2) during Delta and pre-Delta eras in Asia, despite it being a pandemic.**
***Objective*: To study the epidemiological and clinical characteristics of three waves of pediatric COVID-19 infections in a tertiary-care setting in Thailand.**
***Methods*: This retrospective study reviewed all PCR-confirmed pediatric (0-18 years of age) COVID-19 infections between January 13, 2020, and October 31, 2021, in a tertiary care system in Thailand.**
***Results*: 1,019 patients, aged 0.02 - 18 years, 552 (54.2%) male, and 467 (45.8%) female, with a median age of 9.2 years, were enrolled. Asymptomatic cases accounted for 35.7%, of which 106 (18.9%) had abnormal chest X-ray findings. Most cases were classified as having mild clinical symptoms, with only 8 (0.8%) and 4 (0.4%) developing a severe and critical illness, respectively. There were no deaths. The Delta variant appeared more transmissible than previous ones, but we did not see any difference in disease severity. Upper respiratory tract symptoms were predominant, while few cases had lower respiratory tract involvement. The sensitivity and specificity of dyspnea symptoms to predict radiologically confirmed pneumonia were 14% and 95%, respectively, with a likelihood ratio of 3.37. The overall prognosis was good, with only 13 (1.3 %) needing respiratory support. All cases showed clinical improvement with a decent recovery.**
***Conclusion*: Pediatric COVID-19 during the Delta variant predominance era generally appeared more transmissible but benign. One-fifth of cases had pneumonia, but few cases needed respiratory support. Prevention remains important for disease control.**

Keywords: Pediatric; COVID-19; SARS-CoV-2; Delta.

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Introduction. Severe acute respiratory syndrome coronavirus (SARS-CoV-2) and the related disease (COVID-19) were declared a pandemic on March 11, 2020, by the WHO.[1] SARS-CoV-2/COVID-19 arose as an outbreak at the end of 2019 in Wuhan, China, and rapidly spread worldwide.[2,3] SARS-CoV-2/COVID-19 can present as asymptomatic, mild symptoms, severe to critical illness, and can cause death. Morbidity and mortality rates were high among older adults. On the contrary, the infection rate and symptom severity are disproportionately low in children.[4-13]

In Thailand, the first imported case of COVID-19 infection was detected on January 12, 2020, and the first COVID-19 outbreak was in March 2020, with around 100 cases/day. The Department of Disease Control, Ministry of Public Health (DDC MoPH) stated the outbreak was under control after four months due to strict disease prevention measures. However, in December 2020, a second outbreak occurred among foreign workers in Samut Sakhon, a province south of Bangkok, with a maximum of about 1,700 cases/day. Again, the DDC MoPH brought in patient-screening measures in accordance with US CDC guidelines. PUI (Persons Under Investigation) were screened and confined at the early stages, and again, the outbreak was slowed. However, in April 2021, a third wave occurred, the fast-moving Alpha variant, which resulted in a drastically higher infection rate of over 2,000 cases/day.

The situation worsened with the June 2021 Delta variant outbreak in Thailand, with the infection rate reaching more than 20,000 cases/day, with around 0.83% mortality. Delta variant spread rapidly and was more severe, resulting in insufficient medical resources; thus, the government added external health care facilities such as field hospitals and home isolation options. Zoning also began for patients: green (asymptomatic or mild symptoms), yellow (mild dyspnea/high-risk group with mild symptoms), red (clinical pneumonia/oxygen desaturation SpO_2 < 96%/severe symptoms). Green patients went into field hospitals or home isolation, while yellow or red patients were hospitalized. Various successful vaccination campaigns also occurred. With strict public health measures and vaccination coverage, the infection rate gradually declined at the end of October 2021.

In the pediatric context, COVID-19 cases are estimated at < 0.1-15% of all confirmed cases in the first half of 2021.[4-13] In the second half of the year, however, infection grew to 28%[14] in the US, yet the pediatric severe disease rate remains significantly lower compared to adults. Worldwide, pediatric severe cases and deaths are approximately 0.6-5% and 0.3%, respectively.[4-6,8-13] There was limited data on the epidemiological and clinical characteristics of pediatric COVID-19 patients in Thailand.[15,17] Our aim was to study this and compare the clinical characteristics and symptom severity of each wave.

Materials and methods.

Participants. This retrospective study reviewed all PCR-confirmed pediatric (patients aged 0-18 years) COVID-19 infections between January 13, 2020, and October 31, 2021, at Thammasat University Hospital, a university hospital in a province adjacent to Bangkok. Approval for the study was granted by the ethics committee of Thammasat University (MTU-EC-PE-1-293/64). Children with perinatal infection, non-acute COVID-19 infection, and MIS-C (Multisystem inflammatory syndrome in children) were excluded. Initially, all COVID-19 cases were admitted to the hospital, but during the third wave, medical resources were limited; green patients were admitted into field hospitals or home isolation. Hospitalization was reserved for yellow or red patients. All hospitalized patients underwent chest x-ray (CX-R) and complete blood count (CBC); no patient had done computerized tomography. CX-R and other laboratory exams were only performed for the green group if clinically indicated. After discharge, all COVID-19 patients were advised to quarantine at home for 14 days.

Demographic data and clinical information were collected through a manual chart review. An online standardized database was set up using REDCap (Research Electronic Data Capture), with the main coordinating center in Thammasat University. Data were extracted from medical records in the Electronic Public Health Information System (E-PHIS) and entered by experienced pediatricians. Clinical information was collected: underlying medical conditions, nutritional status, clinical history, initial vital signs, laboratory results (hemoglobin, white blood cell, transaminase, C-reactive protein, CX-R), disease severity, medical management, and clinical outcome.

Nutritional statuses were classified into five groups: severe malnutrition, moderate malnutrition, normal, overweight, and obese. For children < 5 years of age, overweight or obesity was defined as weight-for-height > 2 and 3 standard deviations (SD) above the WHO Child Growth Standard median, respectively.[18-19] Children and adolescents aged between 5 and 18 years were defined as

overweight or obese if BMI-for-age was > 1 or 2 SD above the WHO Growth Reference median, respectively.[18-20] Moderate malnutrition was defined as weight-for-height or BMI-for-age between -2 and -3 SD. According to the WHO Child Growth Standard, severe malnutrition was defined as those < -3 SD.[21] Clinical lower respiratory tract signs composing the dyspnea group were defined as a history of dyspnea/shortness of breath, chest pain, tachypnea, and SpO_2 < 95%. To ensure accuracy, CX-R was reviewed independently by three investigators (two radiologists and one pediatric pulmonologist). CX-R categorization was based on the International Expert Consensus Statement from six countries[22] and was divided into four categories: typical, atypical, intermediate, and negative. A final record was made based on the consensus from two out of three investigators.

Disease severity categorization was based on The National Institutes of Health (NIH)[23] classification of five groups: asymptomatic, mild (mild symptoms without pneumonia), moderate (pneumonia without hypoxemia ($SpO_2 \geq 94\%$), or no symptoms but abnormal CX-R), severe (pneumonia with SpO_2 < 94%), or critically ill (acute respiratory distress syndrome or septic shock). Prior to the Omicron variant outbreak, which began after this study, the MoPH recognized three COVID-19 waves in Thailand: first (January 13, 2020 – December 15, 2020), second (December 16, 2020 – March 31, 2021), third (April 1, 2021, to October 31, 2021). Thus, we have classified the confirmed COVID-19 cases into three groups based on the MoPH nationwide surveillance data of SARS-CoV2 variants: Dominant Beta group - diagnosed before April 1, 2021 (no detection rate recorded); Alpha dominant group from April 1, 2021, to June 30, 2021 (detection rate of 65 - 90%); Delta dominant group from July 1, 2021, to October 31, 2021 (detection rate of 62 - 92%).

Statistical analysis. Data were analyzed using STATA for Windows v14.0. Clinical characteristics and laboratory results for continuous data were reported as median with interquartile range (IQR); categorical data were reported as the frequency with percentage. One-way ANOVA, Wilcoxon rank-sum test, and Kruskal-Wallis test were used to compare continuous data; nominal data analysis used a Chi-square test adjusted for multiple comparisons: P-value ≤ 0.05 was considered statistically significant.

Results. A total of 1,040 confirmed pediatric SARS-CoV-2/COVID-19 cases were enrolled. Of this, 21 cases were excluded: incomplete data (7), referred to other hospitals (8), non-acute SARS-CoV-2 infection (1), perinatal infection (4), and MIS-C (1). Among the remaining 1,019 patients, 552 (54.2%) were male with a median age of 9.2 years (0.02-18 years), with the highest prevalence in those aged 5 - 15 years. 555 (54.9%) patients had normal nutritional status with a mean bodyweight of 36.6 kg, while 59 (5.8%) had severe malnutrition, and 194 (19.2%) were obese. Only 7.8% had underlying diseases: chronic lung disease (0.1%), allergies (1.3%), cardiovascular (0.3%), endocrine (0.3%), neurological (0.3%), chronic renal (0.2%), hematological (1.2%), oncological disease (0.2%), and genetic or developmental-behavioral disorders (1.2%). Very few patients had immunocompromised conditions (0.007%). Regarding the source of exposure, 502 (49%) patients reported known exposure information, the most common contact route being household (39.3%), followed by cluster or community (6.6%), neighborhood (1.8%), school (0.7%), and travel (0.1%).

The first pediatric COVID-19 infection at Thammasat Hospital was reported on February 13, 2021. The distribution, peak severity, and baseline demographic data of the 1019 confirmed pediatric COVID-19 cases are shown in **Figure 1** and **Table 1**. In the Beta group, there were 17 patients, Alpha 324 and Delta 678. Baseline demographic data of the three groups did not significantly differ except for the source of exposure (p < 0.001) and the proportion of children in different age groups (p = 0.019). The Alpha and the Delta period had high prevalence in younger age group than the Beta period. The proportion of children younger than one year was higher during the Delta period, while school-age to adolescence was more frequently found in the Beta period. The Delta group frequently reported unknown sources of exposure more than other groups. However, most of them were still household contact from the source of exposure reported. The details are shown in **Table 1**.

The median day from symptom to diagnosis was one day (IQR 0-1 day); the median day from symptom to hospitalization was three days (IQR 2-6 days). Days from symptoms to hospitalization were significantly different among the variants (p < 0.001). 34.3% of patients were admitted into home isolation, 46.5% to field hospital, 18.9% to Thammasat Hospital, with 0.3% to the pediatric intensive care unit (PICU). Most of the cases were admitted to Thammasat Hospital in the Beta period, but the admission site shifted to the field hospital and home isolation during the Alpha and the Delta period. Patients reported as asymptomatic on arrival were 35.7 %. For all symptomatic patients, upper respiratory signs were most common: cough (42%), fever (31%), rhinorrhea (23%), sore throat (13%), anosmia (11.5%), nasal congestion (5.4%), and loss of taste (4.8%). Lower respiratory signs were few: dyspnea or shortness of breath (3%), chest pain (0.8%), tachypnea (3%) and SpO_2 < 95% (0.1%). Severe and critically ill cases had significantly more fever, cough, dyspnea, tachypnea, and SpO_2 < 95% at presentation compared with mild to moderate cases (p < 0.001). Gastrointestinal symptoms

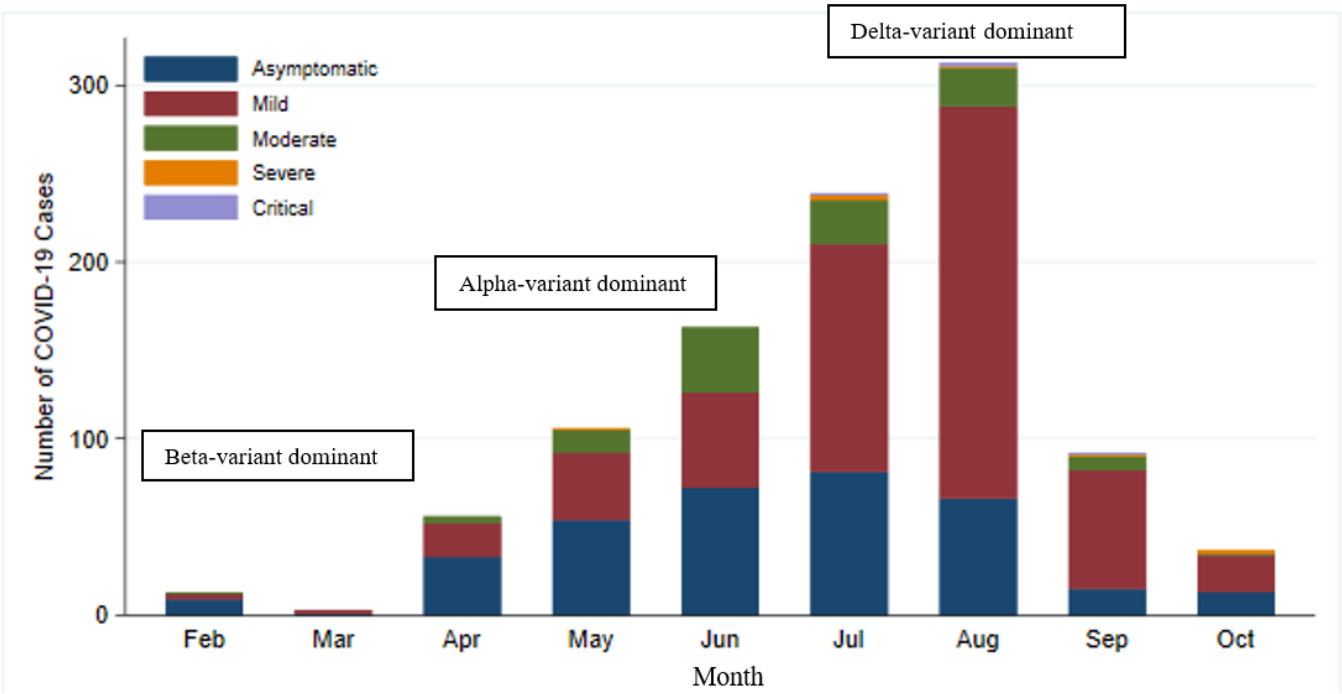

Figure 1. Distribution of 1,019 confirmed pediatric COVID-19 cases at Thammasat Hospital.

Table 1. Baseline demographic data for the three waves of confirmed pediatric COVID-19 cases.

Variable	All cases (N=1019)	Dominant variant group			*p*-value
		Beta (N =17)	Alpha (N=324)	Delta (N=678)	
Male	552 (54.2)	11 (64.7)	163 (50.3)	378 (55.8)	0.177
Age group - < 1 year - 1 year - < 5 years - 5 years - < 10 years - 10 years - < 15 years - ≥ 15 years	 63 (6.18) 206 (20.2) 281(27.6) 273 (26.8) 196 (19.2)	 1 (5.9) 1 (5.9) 2 (11.8) 5 (29.4) 8 (47.1)	 12 (3.7) 65 (20.1) 84 (25.9) 94 (29.0) 69 (21.3)	 50 (7.4) 140 (20.6) 195 (28.8) 174 (25.7) 119 (17.6)	0.019
Nutritional status - Severe malnutrition - Moderate malnutrition - Normal - Overweight - Obese	N=1011 59 (5.8) 54 (5.3) 555 (54.9) 149 (14.7) 194 (19.2)	N = 14 1 (7.1) 0 9 (64.3) 2 (14.3) 2 (14.3)	N = 322 15 (4.7) 14 (4.4) 198 (61.5) 43 (13.4) 52 (16.2)	N = 675 43 (6.4) 39 (5.8) 347 (51.4) 103 (15.3) 143 (21.2)	0.226
Source of exposure - Unknown source - Household contact - Cluster/community - Other	N =1,010 517 (51.2) 397(39.3) 67 (6.6) 29 (2.9)	N = 17 4 (23.5) 10 (58.8) 2 (11.8) 1 (5.9)	N = 319 94 (29.4) 173 (54.2) 41 (12.8) 11 (3.4)	N = 674 419 (62.1) 214 (31.7) 24 (3.6) 17 (2.5)	<0.001
Underlying diseases - None - Chronic lung disease - Allergic disease - Cardiovascular disease - Neurologic disease - Chronic renal disease - Hematologic disease - Oncology - Genetic/DBP	 940 (92.3) 1 (0.1) 13 (1.3) 3 (0.3) 3 (0.3) 2 (0.2) 12 (1.2) 2 (0.2) 12 (1.2)	 15 (88.2) 0 0 0 0 0 1 (5.9) 0 0	 306 (94.4) 0 3 (0.9) 1 (0.3) 0 0 7 (2.2) 0 2 (0.6)	 619 (91.3) 1 (0.2) 10 (1.5) 2 (0.3) 3 (0.4) 2 (0.3) 24 (3.5) 2 (0.3) 10 (1.5)	 0.180 0.777 0.688 0.974 0.469 0.604 0.407 0.604 0.451
Immunocompromised host	7(0.007)	0	3 (17.6)	4 (6.8)	0.348

Categorical variables presented as count (percentage); *p* values show differences between 3 waves. DBP = developmental & behavioral disorder
Other source of exposure = exposure via neighborhood, school, hospital, travel.

included diarrhea (7.3%), vomiting (2.1%), and abdominal pain (0.9%). Other symptoms were headache (7.1%), fatigue (2.1%), myalgia/arthralgia (1.5%), rash (2%), numbness (0.2%) and palpitation (0.3%). Clinical manifestations were also significantly different among the variants. During the Delta variant group, there was a

significantly lower number of asymptomatic patients compared to the other two groups ($p < 0.001$). Nevertheless, most of the symptomatic patients had only mild symptoms, including fever, cough, rhinorrhea, sore throat, anosmia, and loss of taste. In the Beta and the Alpha period, most cases were asymptomatic. The Beta group was found to have more prominent lower respiratory tract signs than the other groups. Only 1% had desaturation on arrival, with no significant difference between groups. For extra-respiratory tract symptoms, diarrhea and headache were frequently found in the Beta and the Delta period compared to the Alpha period with $p = 0.002$ and 0.031, respectively. Fatigue and myalgia were more prominent in the Beta period ($p \leq 0.001$) (**Table2**).

Table 2 Clinical characteristics and laboratory results throughout the three waves.

Variable	All cases (N=1019)	Dominant variant group			*p*-value
		Beta (N =17)	Alpha (N=324)	Delta (N=678)	
Day from symptom-to-diagnosis	1 (0,1)	0 (0,0)	0 (0,1)	1 (0,1)	< 0.001
Day from symptom-to-hospitalization	3 (2,6)	3 (1,4)	5 (2,6)	2(2,5)	< 0.001
Hospitalization					
- Home isolation	349 (34.3)	1 (5.9)	0	348 (51.4)	
- Field hospital	473 (46.5)	7(41.2)	212 (65.4)	254 (37.5)	< 0.001
- Hospital	193 (18.9)	9 (52.9)	112 (34.6)	72 (10.6)	
- PICU	3 (0.3)	0	0	3 (0.4)	
Clinical manifestations					
- No symptoms	364 (35.7)	10 (58.8)	186 (57.4)	168 (24.8)	<0.001
- Fever	317 (31.1)	1 (5.9)	51 (15.7)	317 (31.1)	<0.001
- Cough	432 (42.4)	4 (23.5)	106 (32.7)	322 (47.5)	<0.001
- Rhinorrhea	235 (23.1)	5 (29.4)	45 (13.9)	185 (27.3)	< 0.001
- Nasal congestion	55 (5.4)	2 (11.8)	6 (1.9)	47 (6.9)	0.002
- Sore throat	132 (12.9)	1 (5.9)	14 (4.3)	117 (17.3)	< 0.001
- Anosmia	117 (11.5)	1 (5.9)	13 (4.0)	103 (15.2)	< 0.001
- Loss of taste	49 (4.8)	0	6 (1.9)	43 (6.3)	0.005
- Dyspnea	31 (3.0)	2 (11.8)	5 (1.5)	24 (3.5)	0.024
- Chest pain	8 (0.8)	0	3 (0.9)	5 (0.7)	0.888
- Palpitation	3 (0.3)	0	1 (0.3)	2 (0.3)	0.974
- Diarrhea	74 (7.3)	2 (11.8)	10 (3.1)	62 (9.1)	0.002
- Vomiting	21 (2.1)	0	4 (1.2)	17 (2.5)	0.346
- Abdominal pain	9 (0.9)	0	1 (0.3)	8 (1.2)	0.358
- Fatigue	21 (2.1)	3 (17.7)	3 (0.9)	15 (2.2)	< 0.001
- Headache/vertigo	72 (7.1)	1 (5.9)	13 (4.0)	58 (8.6)	0.031
- Myalgia/arthralgia	15 (1.5)	2 (11.8)	2 (0.6)	11 (1.6)	0.001
- Rash	20 (1.9)	0	2 (0.6)	18 (2.6)	0.079
- Numbness	2 (0.2)	0	0	2 (0.3)	0.604
Vital signs					
- BT $\geq$ 37.5^{o}C	108 (10.6)	1 (5.9)	27 (8.3)	80 (11.8)	0.208
- Tachycardia for age	21(2.1)	4 (23.5)	5 (1.5)	12 (1.8)	< 0.001
- Tachypnea for age	31(3)	3 (17.7)	14 (4.3)	14 (2.1)	< 0.001
Desaturation	10(1)	0	1 (0.3)	9 (1.3)	0.285
CBC	(N=431)	(N=11)	(N = 152)	(N = 268)	
- Hemoglobin (g/dl)	12.8 (11.9, 13.7)	14.1 (12.1, 15.6)	12.6 (11.6, 13.4)	12.8 (12, 13.7)	0.028
- Hct (%)	38.9 (36, 41)	42.8 (37.5, 47.2)	38.4 (35.8, 40.7)	39.3 (36.8, 41.8)	0.005
- Wbc (x10^{9}/L)	6 (4.7,7.9)	5.8 (4.9, 7.6)	6.0 (4.8, 7.9)	5.95 (4.5, 8.1)	0.945
- Neutrophil (%)	38.8 (28, 50)	44.3 (36.3, 56)	38.9 (30.1, 49.2)	38.1 (27.9, 50.4)	0.685
- Lymphocyte (%)	47.3 (37, 58)	45.9 (35, 53.1)	47.6 (37.3, 58)	47.5 (35.6, 58.9)	0.857
- Platelet (x10^{9}/L)	265((219,319)	286 (239, 327)	266 (223, 311)	263 (216, 321)	0.745
Liver function test	(N=172)	(N = 4)	(N = 46)	(N = 122)	
- AST (U/L) (N=172)	25 (21, 23)	19.5(17.5, 28)	24 (20, 30)	26 (21, 37)	0.162
- ALT (U/L) (N=172)	15 (11, 15)	13 (9.5, 14.5)	15 (12. 21)	15 (10, 27)	0.557
Acute phase reactant	(N=35)		(N = 13)	(N = 22)	
- CRP (mg/L)	2.32(0.43, 11.6)	-	1.74(0.23, 4.14)	2.69(0.5, 18)	0.206
Chest X-ray	(N 559)	(N = 12)	(N = 192)	(N = 355)	0.973
Abnormal	106 (18.9)	2 (16.7)	36 (18.7)	68 (19.2)	
Disease severity	(N=1019)	(N = 17)	(N = 324)	(N = 678)	
- Asymptomatic	343(33.7)	11 (64.7)	159 (49.1)	173 (25.5)	
- Mild	553(54.27)	5 (29.4)	109 (33.6)	439 (64.7)	<0.001
- Moderate	111(10.9)	1 (5.9)	55 (16.9)	55 (8.1)	
- Severe	8(0.8)	0	1 (0.31)	7 (1.03)	

- Critically ill	4(0.4)	0	0	4 (0.6)	
Received Favipiravir	212(20.8)	2 (11.8)	49 (15.1)	161 (23.7)	0.005
Respiratory equipment - Cannulas - Mask with bag - HHFNC - Ventilator	(N = 13) 4 (30.8) 1(7.7) 4 (30.8) 4 (30.8)	 0 0 0 0	(N = 1) 0 0 1 (100) 0	(N = 13) 4 (30.8) 1 (7.7) 4 (30.8) 4 (30.8)	0.487
Ventilator day	9(5,16)	0	0	9 (5,16)	-
Outcome - Recovery - Complications - Death	(N=1019) 1018(99.9) 1(0.1) 0	(N = 17) 17 (100) 0 0	(N = 324) 324 (100) 0 0	(N = 678) 677 (99.9) 1 (0.1) 0	0.777

Categorical variables are presented as count (percentage). Continuous variables are presented as median (interquartile range; IQR). p values show differences between three outbreaks.

Among cases with laboratory investigations, the median hemoglobin was 12.8 (IQR 11.9 - 13.7 g/dl), the median white blood cell counts were 6 x 10^9/L (IQR 4.7-7.9 x 10^9/L) with the median neutrophils count of 39 (IQR 28 - 50%), median lymphocyte counts of 47 (IQR 37 - 58%), and median platelet counts of 265 x 10^9/L (IQR 219-319 x 10^9/L), the median AST was 25 (IQR 21 - 23 U/L), median ALT of 15 (IQR 11 - 15 U/L), and median CRP of 2.3 (IQR 0.4 - 11.6 mg/L). CX-R and laboratory investigations data did not significantly differ among variants, except for the highest hemoglobin level during the Beta period. These data were demonstrated in **Tables 2** and **3**.

CX-R and laboratory investigations were not routine. Only 564 patients (55.3%) had CX-R, and among them, 106 (18.8%) had abnormal findings: 81% patchy or ground-glass opacities, 16% interstitial, and 2.9% nodular. For abnormal distribution, 62% had peripheral infiltration, 37% central, 46% unilateral, 35% bilateral and 19% multifocal. Two cases had atelectasis, and one had a pneumothorax. We attempted to correlate abnormal CX-R findings with lower respiratory tract signs (dyspnea symptoms). Abnormal CX-R results were more likely found in patients with dyspnea than in non-dyspnea patients (44 vs. 17%; $p < 0.0001$). When we evaluated dyspnea symptoms for prediction of pneumonia (abnormal CXR), there was low sensitivity of 14% (95% CI, 8.1 - 22.3) but high specificity of 95% (95% CI, 93.5 - 97.5), with the likelihood ratio being 3.37 (95% CI, 1.77 - 85.8). Positive predictive value was 44% (95% CI, 27.2 - 62.1), and negative predictive value was 82.8% (95% CI, 79.15 - 85.8). Details are shown in **Table 3**.

Within the 1,019 patients, asymptomatic cases were 33.7%, mild symptoms 54.3%, moderate 10.9%, severe 0.8%, and critically ill 0.4%. The proportion of patients with underlying conditions was significantly higher in severe/critically-ill patients when compared to the non-severe groups (7.5% vs. 0.6%; $p < 0.001$). Patients beyond infancy tended to be more asymptomatic than infants (35% vs. 13%; P < 0.001), and the infant group were more likely to have critical illness than other groups (1.6% vs. 0.39%; p =0.001). We also found that the severe group patient had more lymphopenia than the mild to moderate group (26 % vs. 46%; p = 0.001). Among severe cases, 5 (38%) patients required low-flow oxygen, 4 (31%) needed humidified high-flow nasal cannulas (HHFNC), and 4 (31%) required invasive ventilation. All showed clinical improvement with full recovery except for one case which experienced neurological sequelae due to venous sinus thrombosis. We had no deaths. Compared among groups, symptomatic patients were more likely to be found in the Delta group ($p < 0.001$), but most cases presented with mild upper respiratory tract symptoms. We saw no significant differences in each wave for the moderate to severe and critically ill groups. There was a slight increase in severity from Beta to Alpha, Delta dominant groups. Critically ill patients were found only during the Delta period. The details are shown in **Table 2**.

Table 3 Accuracy of dyspnea symptoms with pneumonia as detected by abnormal CXR.

Results of dyspnea	Abnormal CXR	Normal CXR	Total
Positive	15 (44%)	19 (55%)	34
Negative	91 (17%)	439 (82.8%)	530
Total	106 (18.8%)	458 (81.2%)	564
Sensitivity 14% (15/106; 95% CI, 8.1 - 22.3) Specificity 95% (439/458; 95% CI, 93.5 - 97.5) Positive predictive value 44% (15/34; 95% CI, 27.2 - 62.1) Negative predictive value 82.8% (439/530; 95% CI, 79.15 - 85.8) Likelihood ratio 3.37 (15/106:19/458; 95% CI ,1.77 - 85.8)			

Dyspnea symptoms = dyspnea, shortness of breath, chest pain and oxygen desaturation (SpO2 < 95%).

Discussion. Our study described the epidemiological and clinical characteristics of pediatric COVID-19 infection cases in our Thai tertiary care center. We found that pediatric COVID-19 was not severe, with severe and critical illness rates being only 0.8 and 0.4%, respectively. This seemed less dire than previous studies reporting severe/critical pediatric cases at around 0.8 - 5.3%.[4-6,8-13] We also observed a decrease in asymptomatic infections in the Delta dominant group compared to the Alpha one (24.8% vs. 57.4 %). However, most symptomatic patients had mild upper respiratory tract symptoms, and no significant changes appeared in regard to severe disease. Our data was in line with Byung-Han R et al.,[24] their asymptomatic Delta group being 29.3% and their non-Delta group 43.4%.

Interestingly, Delta variants did not appear to demonstrate worse clinical outcomes than prior lineages since most patients were classified as having mild to moderate symptoms. Delahoy et al.[25] also reported increased ER visits and hospitalizations, especially in unvaccinated children, during the Delta wave, but indicators of severe disease (ICU admission, receiving invasive mechanical ventilation, or death) did not significantly increase from the previous outbreaks. Their study concluded that the Delta variant was more transmissible than the previously circulating SARS-CoV-2 variants; however, it remains uncertain whether it causes more severe disease.

There was no significant change in the proportion of the severe disease among groups for the disease severity. Nevertheless, we found interesting data that no severe case was found despite a higher proportion of patients presenting with lower respiratory tract signs during the Beta period. More severe/critically-ill patients were seen during the Delta versus the pre-Delta period. This might be due to the high transmissibility combined with limited medical resources, resulting in delayed hospitalization and treatment. However, after the Thai government added additional health care facilities in the Alpha and the Delta period to enhance access to medical care, more patients were readily cared for in the field hospital and home isolation. The government then implemented preventive measures in vaccination campaigns and media knowledge sharing. As a result, the situation improved, especially regarding day-of-symptoms-to-hospitalization data and the infection rate, which gradually declined during the end of the Delta season. Preventive measures, including vaccination of those eligible, universal mask-wearing, social distancing, and quarantining after exposure to persons with COVID-19, appeared to have worked and remain important for disease control.

We found slightly more males than females afflicted, consistently with previous studies.[4,6,8,16,24] However, no significant gender difference was observed in our study. The median age was 9.2 years (2 months - 18 years), with the highest prevalence in children aged 5-15, suggesting that COVID-19 occurs throughout childhood. For source of exposure, due to the wide community transmission during the Delta period, it was not feasible to trace the source of exposure in most patients. Most contacts were from the household in the cases with a known exposure, followed by cluster/community. Especially in the Alpha dominant group, the infection started in a boxing stadium and certain pubs in downtown Bangkok, which implies the possibility of person-to-person transmission in any closed environment. This was the start of strict social distancing measures imposed by the government. Most patients had no comorbidities in our study, but we found that significantly more severe/critically-ill patients had underlying conditions. One with congenital heart disease case developed venous sinus thrombosis with acute respiratory failure after COVID-19 infection and needed special care in the PICU. Finally, the patient was discharged with anticoagulants, and the neurological deficit slightly improved. However, when diseases were analyzed separately into risk groups, including asthma, chronic lung disease, congenital heart disease, oncology, and obesity, the findings show that none of these diseases had any severe effects.

The prevalence of asymptomatic pediatric patients with COVID-19 was 35.7%, higher than other studies reporting 1.3% - 40%.[4-6,8-13] This percentage varied with time and space. Upper respiratory tract signs were common for symptomatic patients, while lower respiratory tract signs were found less frequently. Patients who had lower respiratory tract issues seemed to have more severe diseases. When we evaluated dyspnea symptoms in order to predict pneumonia, we found low sensitivity (14%), high specificity (95%), and low positive predictive value (44%) but a high negative predictive value (82.8%), with a likelihood ratio of 3.37. The dyspnea symptoms were not a good screening test for predicting pneumonia, although patients with dyspnea symptoms had significantly abnormal CX-R more often than those without. We also found that non-dyspnea patients usually had normal CX-R. Therefore, we suggested that CX-R should be done in dyspnea cases, but we cautioned that it might not be necessary for non-dyspnea patients. In our study, the low positive predictive value might be explained by the low sensitivity of dyspnea symptoms to predict pneumonia and the low prevalence of pneumonia in pediatric COVID-19 infections. In areas with a high prevalence of pneumonia, the positive predictive value might be higher.

We had seen little data on the clinical characteristics of pediatric COVID-19 in Asia, especially during the Delta variant wave. In our study's favor, we had access to a large population in our tertiary care hospital, so we were able to compare clinical characteristics during three different outbreaks and strains of COVID-19. According to our data, the overall disease severity of pediatric

COVID-19 was low, but with a rapid increase in the number of cases, we received more patients with severe and critical illnesses during the Delta versus the pre-Delta period. The mutation variants may be linked to greater transmissibility, increased risk of reinfection, and severe disease. Therefore, preventive measures, including vaccination of those eligible, universal mask-wearing, and social distancing, should be warranted for disease control. In October 2021 (At the end of this research), the vaccination campaign for children older than 12 was initiated to reduce disease transmission and limit the new cases of severe disease.

Despite the favors, we had some limitations. First, as this was a retrospective study, there was the possibility that some records might not be complete as some might be collected via phone call and relied on respondent recall. Data such as body weight, height, symptom time span before admission to health care unit, source of contact, etc., might not be accurate. Secondly, most patients were treated in an isolated room or cohort ward, and the treatment was usually done by telemedicine; therefore, there would be limitations in physical examination. As a result, the diagnosis of pneumonia can only be based on the history of dyspnea, tachypnea for age, desaturation, and abnormal CX-R, leading to more CX-R being performed than normal. Thirdly, during all three outbreaks, particularly in the Delta wave, there was an overload of cases in the health care systems, resulting in delayed treatment leading to greater severity. Finally, our study did not confirm data on the SARS-CoV-2 strains. We relied on the nationwide surveillance data of SAR-CoV2 variants from the MoPH Thailand to determine when and where the strains were predominantly active.

Conclusions. The epidemiological and clinical characteristics of pediatric COVID-19 cases in our tertiary care center in Thailand were similar to previous reports. COVID-19 occurs in all ages of childhood, with no gender difference. Most cases presented as mild upper respiratory tract symptoms. However, infants were vulnerable to COVID-19 infection. The Delta variant is more transmissible than previous ones, but we saw no difference in disease severity compared to pre-Delta waves.

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