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Research Article

การศึกษาลักษณะทางคลินิกของผู้ป่วยเด็กติดเชื้อโควิด-19 อายุน้อยกว่า 15 ปี ที่เข้ารับการรักษาที่โรงพยาบาลเจริญกรุงประชารักษ์

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บทคัดย่อ

วัตถุประสงค์: เพื่อศึกษาอาการแสดงทางคลินิก และผลการรักษาผู้ป่วยเด็กที่ติดโควิด-19 (เชื้อ SARS-CoV-2) และเปรียบเทียบระหว่าง 3 ระลอกการระบาด

วิธีดำเนินการวิจัย: ศึกษาย้อนหลังโดยรวบรวมข้อมูลผู้ป่วยอายุต่ำกว่า 15 ปี ที่ได้รับการวินิจฉัยยืนยันติดเชื้อ SARS-CoV-2 ตั้งแต่วันที่ 13 มกราคม พ.ศ. 2563 ถึงวันที่ 15 พฤษภาคม พ.ศ. 2565 โดยจำแนกสายพันธุ์ SARS-CoV-2 ตามกรมควบคุมโรค ออกเป็นระยะก่อนเดลต้า (pre-Delta), เดลต้า (Delta) และโอมิครอน (Omicron)

ผลการวิจัย: ผู้ป่วยเด็กทั้งหมด 895 ราย เพศชาย ร้อยละ 55.8 อายุเฉลี่ย (ส่วนเบี่ยงเบนมาตรฐาน) 7.35 (± 4.6) ปี มีโรคประจำตัว ร้อยละ 4.7 โดยโรคทางเดินหายใจเป็นโรคที่พบมากที่สุด ร้อยละ 2.6 พบการติดเชื้อจากคนในครอบครัว ร้อยละ 65.8 อาการทางคลินิกที่พบ ได้แก่ อาการทางเดินหายใจส่วนบน (ไอ น้ำมูก มีเสมหะ และเจ็บคอ เป็นร้อยละ 55.9, 37.8, 13.2 และ 23.1 ตามลำดับ) ไข้ ร้อยละ 57 และอาการทางระบบอื่น ๆ เช่น ระบบทางเดินอาหาร (ถ่ายอุจจาระเหลว และคลื่นไส้/อาเจียน เป็นร้อยละ 10.2 และ 8.4) ชัก ร้อยละ 3.7 และพบผู้ป่วยไม่แสดงอาการทางคลินิก ร้อยละ 13.5 ระดับความรุนแรงของโรคแบ่งเป็น ไม่มีอาการ ความรุนแรงเล็กน้อย ความรุนแรงปานกลาง และอาการรุนแรง เป็นร้อยละ 8.8, 55, 34.9 และ 1.3 ตามลำดับ เมื่อเปรียบเทียบระหว่างสายพันธุ์ พบว่า สายพันธุ์โอมิครอน มีไข้สูงและอาการชักเด่นชัดกว่า ขณะที่สายพันธุ์เดลต้า มีอาการสูญเสียการรับรสและกลิ่น ส่วนในช่วงก่อนเดลต้า ส่วนใหญ่ไม่มีอาการ การตรวจภาพถ่ายรังสีทรวงอก พบความผิดปกติ ร้อยละ 38.5 โดยเป็นแบบระหว่างเนื้อเยื่อช่องว่างปอด (interstitial) ร้อยละ 76.8 และแบบกระจายเป็นหย่อม ๆ (patchy) หรือภาวะฝ้าหรือมัวคล้ายกระจกฝ้า (ground glass opacity) ร้อยละ 29.8 ผู้ป่วยที่มีอาการและ/หรือมีปัจจัยเสี่ยงได้รับการรักษาด้วยยาฟาวิพิราเวียร์ (favipiravir) ร้อยละ 83.3 ผู้ป่วยพบการดำเนินโรคที่รุนแรงขึ้น ร้อยละ 4.9 และได้รับออกซิเจนเสริม ร้อยละ 1.3 แต่ไม่มีรายใดต้องใส่ท่อช่วยหายใจ ผลลัพธ์โดยรวมพบว่า ผู้ป่วยทั้งหมดหายเป็นปกติ ไม่มีรายงานการเสียชีวิต

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บทคัดย่อ (ต่อ)

สรุป: การติดเชื้อโควิด -19 ในเด็กโดยทั่วไปมีพยากรณ์โรคที่ดี อาการทางเดินหายใจเป็นอาการที่พบได้บ่อยที่สุด แต่ในแต่ละช่วงเวลาของสายพันธุ์จะมีอาการเด่นที่แตกต่างกัน ผู้ป่วยส่วนใหญ่อาการดีขึ้นเป็นปกติ

คำสำคัญ: เด็ก ไวรัสซาร์ส-โควี-2 โควิด-19 เดลต้า โอมิครอน

บทความวิจัย
Research Article

Clinical characteristics of pediatric COVID-19 infection in patients aged under 15 years visiting Charoenkrung Pracharak Hospital

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Abstract

Objectives: To study the clinical presentation and treatment outcomes of pediatric SARS-CoV-2 infection and differentiate across three variants in Bangkok Metropolitan Hospitals.

Materials and Methods: This retrospective study reviewed pediatric patients under 15 years old with confirmed SARS-CoV-2 infection from January 2020 to June 2022. The SARS-CoV-2 variants were defined on the basis of the epidemic curve provided by the Department of Disease Control.

Results: A total of 895 pediatric SARS-CoV-2 infection cases were enrolled, of which 55.8% were male. The mean age (SD) was 7.35 (±4.6) years old, and 4.7% of patients had underlying diseases, with respiratory diseases being the most common (2.6%). Household contact cases accounted for 65.8% of the total. Clinical presentations included upper respiratory symptoms (cough 55.9%, rhinorrhea 37.8%, sputum 13.2%, sore throat 23.1%), fever (57%), and extra-pulmonary tract symptoms (e.g., gastrointestinal symptoms such as diarrhea 10.2% and nausea/vomiting 8.4%) and seizure 3.7%, with 13.5% showing no symptoms. The disease spectrum included asymptomatic 8.8%, mild severity 55%, moderate severity 34.9% and severe severity 1.3%. Comparing the three periods; pre-Delta, Delta, and Omicron variants; high-grade fever and seizures predominated in Omicron, while anosmia and loss of taste were notable in Delta, while the pre-Delta period predominantly had asymptomatic cases. Chest x-rays of the patients revealed abnormalities in 38.5% of cases. Abnormal chest radiography showed that interstitial infiltration was 76.8% and patchy infiltration or ground glass opacity were 29.8%. Favipiravir was prescribed to 83.3% of children with symptomatic COVID-19 and/or risk factors. Disease progression was observed in 4.9% of cases, with 1.3% requiring oxygen therapy, and none needing mechanical ventilation. Overall, all patients fully recovered, with no mortality reported.

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Abstract (cont.)

Conclusion: Pediatric COVID-19 infection generally has a favorable prognosis in children. Although respiratory symptoms are the most common presentation, each period may have different predominant symptoms. Overall, patients typically experience full recovery.

Keywords: pediatric, SARS-CoV-2, COVID-19, Delta, Omicron

Introduction

Novel Coronavirus Disease 2019 (COVID-19) is caused by the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2). In early December 2019, coronavirus infection emerged and rapidly spread worldwide. The World Health Organization (WHO) declared the coronavirus outbreak a pandemic on March 11th, 2020.[1] The American Academy of Pediatrics and the Children's Hospital Association (AAP) reported the cumulative number of children with SARS-CoV-2 infection up to 338,982 cases. Children represented 8.8% of all cases and the mortality rate was 0.8% (reported in July 2020).[2]

The first report of SARS-CoV-2 virus infection in Thailand was in January 2020. Recently, Thailand had a SARS-CoV-2 infection outbreak which continued spreading. According to the Department of Disease Control, Ministry of Public Health (DDC MoPH), there are 5 variants of SAR-CoV-2 which are the Wuhan (S), GS, Alpha, Delta, and Omicron variants. The government set-up the health care system for disease control and announced clinical practice guidelines for COVID-19 (Thai CPG COVID-19 guidelines).[3]

Charoenkrung Pracharak Hospital (CKP Hospital) is a tertiary care center with a capacity of 500 beds, including 30 designated for children and 7 for critically ill pediatric patients. It also serves as a referral center for the southern districts of Bangkok. CKP Hospital reported that pediatric SARS-CoV-2 infections accounted for 7.3% of all confirmed COVID-19 cases. Pediatricians managed these cases according to the Thai Clinical Practice Guidelines (CPG) for COVID-19.[3] These guidelines have undergone revisions in response to the evolving knowledge of SARS-CoV-2 infection, particularly with respect to classification of disease severity and treatment approaches. The recommended antiviral treatments for pediatric patients have primarily included favipiravir and remdesivir. Systemic corticosteroids are indicated for children presenting with pneumonia or severe disease progression.

According to the government policy and Thai CPG COVID-19 guidelines, all pediatric patients who were infected with the SARS-CoV-2 virus were admitted into either a hospital ward, Pediatric Intensive Care Unit (PICU), field hospital, community isolation, or home isolation based on the risk factors and disease severity of the patients. The children with asymptomatic infection or mild severity were admitted to field hospitals, community isolation, or home isolation, while the children with moderate severity or with risk factors were admitted to a hospital ward or PICU.

Since SARS-CoV-2 infection is a new emerging disease, studies of clinical presentation and treatment outcomes in children in Thailand are limited. There have been few studies that examined the clinical presentation in children with SARS-CoV-2 infection and compared between clinical presentations in each variant.[4-7]

Objectives

The primary objective of this study was to describe the clinical characteristics and treatment outcomes for pediatric SARS-CoV-2 in a tertiary care center. The secondary objective was to compare the differences in clinical characteristics and

severity in each variant according to the epidemic curve from the DDC MoPH, Thailand.

Materials and Methods

Study protocol

A retrospective descriptive study reviewed all pediatric cases (aged 0-15 years old) which were admitted with SARS-CoV-2 virus infection to CKP Hospital, field hospitals, community isolation, and home isolation programs during January 13th, 2020 to May 15th, 2022. All children were diagnosed using confirmatory tests of Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) and/or Antigen Test Kits (ATKs) confirming SARS-CoV-2 infection. Children with perinatal infection, Multi-inflammatory Syndrome in Children (MIS-C), incomplete data collection, and incidental findings such as pre-operative diagnosis were excluded. The study protocol was approved by the BMA Human Research Ethics Committee (BMAHREC), approval number R005h/65_EXP.

Data collection

All demographic data, clinical presentations, chest radiographs, and outcomes were collected through manual chart review. The online database was extracted from medical records in the Electronic Public Health Information System (E-PHIS) at Charoenkrung Pracharak Hospital and reviewed by pediatricians. A google sheet was set up to record the data information.

Definitions

The risk factors for severe disease followed Thai CPG COVID-19 guidelines[3] that categorized patients aged under 1 year old, obesity those who had Weight-For-Height (WFH) > 140% following the Nutritional Association of Thailand,[8] respiratory disease (e.g., chronic lung disease and asthma), cardiovascular disease (e.g., congenital heart disease), neurological systems (e.g., cerebral palsy and epilepsy), nephrological disease (e.g., chronic kidney disease), immunological disease (e.g., cancer and immune deficiency), diabetes mellitus, and genetic disease (e.g., Down syndrome). The severity of disease as shown on the Table 1.

Chest radiography was performed in almost all cases who visited the hospital for the purpose of screening. The chest radiography was reviewed and reported by attending radiologists. Following the Department of Disease Control Ministry of Public Health Thailand guidelines, this study classified SARS-CoV-2 infection into three periods: pre-Delta variant (Wuhan (S), G, and Alpha) from January 13th, 2020 to June 30th, 2021; Delta variant from July 1st, 2021 to December 31st, 2021, and Omicron variant from January 1st, 2022 to May 15th, 2022.

Table 1 The severity of disease was adapted from the World Health Organization 2021[9]

Severity of SARS-CoV-2 infection	Signs and symptoms
1. Asymptomatic	No symptoms
2. Mild COVID-19	Signs and symptoms of respiratory tract infection or gastrointestinal tract symptoms without pneumonia or hypoxia
3. Moderate COVID-19	Pneumonia without signs of severe COVID-19 or asymptomatic with abnormal chest radiography
4. Severe COVID-19	Pneumonia with at least one of following: - Hypoxia (oxygen saturation at room air < 94%) - Tachypnea; > 60 per minute in children < 2 months old ; > 50 per minute in children 2 months old - 1 year old ; > 40 per minute in children 1 - 5 years old ; > 30 per minute in children > 5 years old - Respiratory distress
5. Critical COVID-19	Pneumonia with critical illness (e.g., respiratory failure, shock, cardiac failure, renal failure) requiring mechanical ventilator, inotropes, and vasopressor

Statistical analysis

Data were analyzed using SPSS [version 26 concurrent license]. Qualitative data were analyzed in percentages, while quantitative data were analyzed using means with standard deviation (SD) and medians with Interquartile Range (IQR). For comparisons, we employed ANOVA for continuous data and the chi-squared test for categorical data. A statistically significant p-value of <0.05 was utilized.

Results

In Charoenkrung Pracharak Hospital, 946 pediatric confirmed SARS-CoV-2 infection cases were enrolled. A total of 51 cases were excluded, including 2 cases of perinatal infection, 40 cases due to incomplete data collection and transfer to other centers, and 9 cases due to pre-operative screening. Finally, 895 cases were analyzed. The patients were diagnosed by RT-PCR in 98.7% of cases and by ATK in 1.3% of cases.

Table 2 Baseline characteristics of pediatric SARS-CoV-2 infection cases at Charoenkrung Pracharak Hospital

Baseline characteristics	Total n = 895	pre-Delta n = 205	Delta n = 354	Omicron n = 336	p-value
Male; n (%)	499(55.8)	141(68.8)	165(46.6)	193(57.4)	<0.001*
Age (year); mean ± SD	7.35±4.6	7.16±4.5	7.78±4.9	7.02±4.5	0.078
Age group; n (%)					
- At birth – 1 year old	73(8.2)	13(6.4)	32(9.0)	28(8.3)	0.526
- 1 - < 5 years old	215(24.0)	55(26.8)	82(23.2)	78(23.2)	0.563
- 5 - < 10 years old	258(28.8)	63(30.7)	76(21.5)	119(35.4)	<0.001*
- 10 - 15 years old	349(39.0)	74(36.1)	164(46.3)	111(33.1)	0.001*
Obese; n (%)	74(8.3)	28(13.7)	34(9.6)	12(3.6)	<0.001*
Underlying disease; n (%)					
- No underlying disease	853(95.3)	192(93.7)	338(95.5)	323(96.1)	0.411
- Respiratory disease	23(2.6)	8(3.9)	9(2.5)	6(1.8)	0.320
- Neurological disease	6(0.7)	1(0.5)	1(0.3)	4(1.2)	0.322
- Cardiovascular disease	5(0.6)	1(0.5)	2(0.6)	2(0.6)	0.987
- Diabetes mellitus	3(0.3)	0	3(0.8)	0	0.100
- Genetic disease	3(0.3)	1(0.5)	1(0.3)	1(0.3)	0.911
- Nephrological disease	2(0.2)	1(0.5)	0	1(0.3)	0.468
- Immunological disease	2(0.2)	2(1.0)	0	0	0.034*
Source of exposure; n (%)					
- Household contact	589(65.8)	160(78.0)	264(74.6)	165(49.1)	<0.001*
- Unknown source	273(30.5)	35(17.1)	77(21.7)	161(47.9)	<0.001*
- Community/cluster	29(3.2)	10(4.9)	11(3.1)	8(2.4)	0.277
- School	4(0.5)	0	2(0.6)	2(0.6)	0.550
Diagnosis; n (%)					
- RT-PCR	883(98.7)	203(99.0)	350(98.9)	330(98.2)	0.661
- ATK	12(1.3)	2(1.0)	4(1.1)	6(1.8)	

* = significance level $p<0.05$ by chi-square, ANOVA, or Kruskal-Wallis test

The baseline characteristics of pediatric SARS-CoV-2 infection cases illustrate on the Table 2. The patients show that 499 (55.8%) were male, with a mean age of 7.35 years old (ranging from 2.7 to 12 years old). The highest prevalence was observed in the age group of children aged 10 to

15 years old. During the Delta period, the prevalence among patients aged 10 to 15 years old was significantly higher compared to other periods, while this period showed significantly lower prevalence among children aged 5 to 10 years old compared to the others. Among the cases, 74 (8.3%) were obese, with a higher prevalence observed in the pre-Delta period than in the Delta and Omicron periods. Among the cases, 95% had no underlying diseases, and there was no difference observed across the three periods. However, 74 (4.7%) patients did have underlying diseases, including respiratory diseases (e.g., asthma and chronic lung disease) in 23 (2.6%) cases, neurological diseases (e.g., epilepsy and cerebral palsy) in 6 (0.7%) cases, cardiovascular diseases (e.g., congenital heart diseases such as VSD and PAVSD) in 5 (0.6%) cases, nephrological diseases (e.g., chronic kidney disease and renal atrophy) in 2 (0.2%) cases, immunological diseases (e.g., immune deficiency and HIV infection) in 2 (0.2%) cases, and genetic diseases (e.g., Pierre Robin syndrome and anorectal malformation) in 3 (0.3%) cases. Regarding the source of exposure, more than half of all exposures were household contacts, accounting for 598 (65.8%) cases, while 273 (30.5%) cases were unknown. In the pre-Delta and Delta periods, the sources of exposure were household contacts at 78% and 74.6%, respectively. However, in the Omicron period, the most common source of exposure was unknown in 47.9% of cases, compared to 17.1% and 21.7% in the pre-Delta and Delta periods, respectively ($p<0.001$).

Table 3 Clinical presentation and severity in pediatric SARS-CoV-2 infection at Charoenkrung Pracharak Hospital in different three periods

Clinical presentation and severity	**Total n = 895**	**pre-Delta n = 205**	**Delta n = 354**	**Omicron n = 336**	**p-value**
Hospitalization; n (%)					
- Field hospital	331(37.0)	69(33.7)	79(22.3)	183(54.5)	<0.001*
- Home isolation	296(33.1)	79(38.5)	175(49.4)	42(12.5)	
- Ward	233(26.0)	56(27.3)	68(19.2)	109(32.4)	
- Community isolation	32(3.6)	0	31(8.8)	1(0.3)	
- PICU	3(0.3)	1(0.5)	1(0.3)	1(0.3)	
Clinical presentations; n (%)					
No symptoms	121(13.5)	44(21.5)	45(12.7)	32(9.5)	<0.001*
Fever	510(57.0)	100(48.8)	194(54.8)	216(64.3)	0.001*

Table 3 Clinical presentation and severity in pediatric SARS-CoV-2 infection at Charoenkrung Pracharak Hospital in different three periods (Cont.)

Clinical presentation and severity	Total n = 895	pre-Delta n = 205	Delta n = 354	Omicron n = 336	p-value
Respiratory tract symptoms					
- Cough	500(55.9)	108(52.7)	196(55.4)	196(58.3)	0.426
- Rhinorrhea	338(37.8)	62(30.2)	170(48.0)	106(31.5)	<0.001*
- Sore throat	207(23.1)	41(20.0)	82(23.2)	84(25.0)	0.408
- Sputum	85(13.2)	22(17.5)	28(15.6)	35(10.4)	0.077
- Anosmia	67(7.5)	14(6.8)	48(13.6)	5(1.5)	<0.001*
Extra-pulmonary symptoms					
- Diarrhea	91(10.2)	23(11.2)	35(9.9)	33(9.8)	0.851
- Nausea vomiting	75(8.4)	5(2.4)	16(4.5)	54(16.1)	<0.001*
- Seizure	33(3.7)	2(1.0)	3(0.8)	28(8.3)	<0.001*
- Rash	27(3.0)	10(4.9)	12(3.4)	5(1.5)	0.071
- Tasteless	25(2.8)	7(3.4)	17(4.8)	1(0.3)	0.001*
- Abdominal pain	10(1.1)	1(0.5)	3(0.8)	6(1.8)	0.312
- Conjunctivitis	4(0.6)	2(1.6)	1(0.6)	1(0.3)	0.289
Vital sign; n (%)					
- Body temperature 37.5-38.5 c	197(22.0)	21(10.2)	55(15.5)	121(36.0)	<0.001*
- Body temperature > 38.5 c	92(10.3)	5(2.4)	25(7.1)	62(18.5)	<0.001*
- Desaturation; SpO_2 < 94 %	6(0.6)	0	1(0.3)	5(1.5)	0.111
- Tachypnea for age	6(0.7)	4(2.0)	2(0.6)	0	0.025*
Disease severity; n (%)					
- Asymptomatic	79(8.8)	30(14.6)	28(7.9)	21(6.3)	<0.001*
- Mild COVID-19	492(55.0)	77(37.6)	182(51.4)	233(69.3)	
- Moderate COVID-19	312(34.9)	94(45.9)	141(39.8)	77(22.9)	
- Severe COVID-19	12(1.3)	4(1.9)	3(0.9)	5(1.5)	
Investigation; n (%)					
Chest radiography	(n=829)	(n=200)	(n=308)	(n=321)	
- Abnormal	319(38.5)	98(49.0)	143(46.4)	78(24.3)	<0.001*
- Interstitial infiltration	245(76.8)	76(77.6)	108(75.5)	61(78.2)	0.883
- Patchy/Ground glass opacity	95(29.8)	30(30.6)	47(32.9)	18(23.1)	0.307

* = significance level p<0.05 by chi-square

Hospitalization data (Table 3) indicate that admissions were distributed as follows: field hospital 37.0%, home isolation 33.1%, ward 26.0%, community isolation 3.6%, and PICU 0.3%. There were significant differences in hospitalization patterns across the three periods. During the pre-delta, Delta, and Omicron periods, patients were primarily admitted to home isolation, accounting for 38.5%, 49.4%, and 12.5% ($p<0.001$), respectively. In contrast, during the Omicron period, the majority of hospitalization occurred in field hospitals 54.5% ($p<0.001$). Additionally, one case was admitted to the PICU ward in each period.

Some patients (13.5%) had no symptoms, while among those who did have symptoms, the most common clinical presentations were fever 57.0%, Upper Respiratory tract Infection (URI) symptoms (cough 55.9%, rhinorrhea 37.8%, sore throat 23.1%, and sputum 13.2%), and extra-pulmonary tract symptoms (e.g., gastrointestinal tract symptoms such as diarrhea 10.2%, and nausea/vomiting 8.4%).

The clinical presentations among the three periods were as follows: in the pre-Delta period, there were predominantly no symptoms compared to the other periods ($p<0.001$). In the Delta period, anosmia, rhinorrhea, and loss of taste were the predominant symptoms ($p<0.001$). Lastly, the Omicron period showed a significant predominance of fever and extra-pulmonary tract symptoms, including seizures and nausea/vomiting, compared to the other two periods ($p<0.001$). For the severity of disease, asymptomatic cases were 8.8%, mild COVID-19 was 55.0%, moderate COVID-19 was 34.9%, and severe COVID-19 was 1.3%. The severity of the disease varied significantly across the three periods. The most prevalent severity in the pre-Delta period was moderate severity, while in the Delta and Omicron periods it was mild severity ($p<0.001$).

The high body temperature and tachypnea exhibited significant differences in each period. Fever and high body temperatures exceeding 38.5 degrees Celsius were predominant in the Omicron period ($p<0.001$), while tachypnea was more prevalent in the Delta period ($p = 0.025$).

Chest radiography was performed in 829 (92.6%) cases, revealing abnormalities in 319 (38.5%) patients. The patients who had categorized in moderate severity and abnormal chest radiography with asymptomatic were 27 (3.2%) cases. Radiological findings illustrated that interstitial infiltration was present in 275 (76.8%) cases, while patchy infiltration or ground glass appearance were found in 95 (29.8%) cases. Abnormal chest radiography findings were lower in the Omicron period compared to the other two periods ($p<0.001$). Additionally, chest radiography did not detect atelectasis or pneumothorax.

Table 4 Treatment and outcomes in pediatric SARS-CoV-2 infection at Charoenkrung Pracharak Hospital in different three periods

Treatment and outcome	Total n = 895	pre-Delta n = 205	Delta n = 354	Omicron n = 336	p-value
Medication; n (%)					
- Received favipiravir					
5 days	734(82.0)	151(73.6)	301(85.0)	282(83.9)	0.001*
10 days	12(1.3)	2(1.0)	8(2.3)	2(0.6)	
- Received steroid	13(1.5)	7(3.4)	5(1.4)	1(0.3)	0.013*
Respiratory equipment; n (%)					
- O_2 cannula	12(1.3)	2(1.0)	4(1.1)	6(1.8)	0.661
- High-flow nasal cannula	0	0	0	0	
- Ventilator	0	0	0	0	
Disease progression; n (%)	44(4.9)	11(5.4)	21(5.9)	12(3.6)	0.338
Outcome; n (%)					
- Recovery	895(100.0)	205(100.0)	354(100.0)	336(100.0)	0
- Complication	0	0	0	0	
- Death	0	0	0	0	

* = significance level $p<0.05$ by chi-square

According to clinical symptoms and risk factors, favipiravir was administered for 5 days to the patients in 82% of all cases. Favipiravir was administered to the patients with a significant difference observed in the three periods ($p = 0.001$). In the pre-Delta period, the administration rate was lower at 151 (73.6%), while in the Delta and Omicron periods, it was administered in 301 (85%) and 282 (83.9%) cases, respectively. Only 12 (1.3%) patients received favipiravir for 10 days. Then 13 patients (1.5%) received steroids as part of combined medication. These were given to 7 (3.4%) patients in the pre-Delta period which was significantly higher than in the other periods ($p<0.001$). Only 12 patients (1.3%) required oxygen cannula for respiratory support, and none required heated humidified high-flow nasal cannula or invasive ventilator. A total of 44 patients (4.9%) experienced disease progression characterized by worsening symptoms and the need for additional medication for treatment. However, there were no significant differences in the outcomes among the three periods, indicating that all pediatric patients with SARS-CoV-2 virus infection recovered by the discharge date, with no complications or deaths reported (Table 4).

Discussion

The study demonstrated the epidemiology, clinical characteristics, and treatment outcomes of pediatric SARS-CoV-2 infected patients in Thai tertiary care centers. The upper respiratory tract symptoms remain the most common symptoms in pediatric patients with SARS-CoV-2 infection. Secondary symptoms include fever and extra-pulmonary tract symptoms (e.g., gastrointestinal tract symptoms). Around 13.5% of patients showed no symptoms. These findings appear to be consistent with previous studies.[10-15]

In the Omicron period, fever, seizures, and gastrointestinal tract symptoms were predominantly observed, similar to Taytard J, et al and Wurm J, et al.[16,17] Furthermore, we found that patients under the age of 5 years had seizures at 2.2%, while those older than 5 years had seizures at 1.4%, indicating lower rates of seizure compared to Katsuta T, et al[18], who revealed that during the Omicron period, the percentage of patients experiencing seizures was 13.4% in the age group of 1-4 years old and 7.4% in the age group of 5-11 years old. The seizure presentation in Omicron correlated with higher body temperatures during this period before the seizure onset. Due to isolation precautions for emerging diseases and practical guidelines of fever with seizure, lumbar puncture was not performed for diagnosis in SARS-CoV-2 meningitis or meningoencephalitis. However, the patients had no other abnormal neurological symptoms and had normal neurological examinations. All of them fully recovered.

The disease severity was mild 55% and moderate 34.9%, which correlates with the findings of the study by Anugularuengkitt S, et al.[6] Severe and critical illness in our study was found in only 1.3%; the severe cases were same as in the studies of Badal S, et al, Irfan O, et al, and Kainth MK, et al[10-12], which reported 0.8-5%. This may be due to early empirical antiviral therapy following Thai guidelines, as 83% of our patients received Favipiravir. In the pre-Delta period, there was a higher prevalence of moderate severity than in the Omicron period and in the work of Satdhabudha A, et al.[5] Due to the early screening using chest radiography, abnormal findings were detected even in asymptomatic patients, leading to their classification into the moderate severity group. Among patients categorized as having moderate severity, the asymptomatic patients who had abnormal chest radiography were 27 cases.

The chest radiography showed abnormal results 38.5%, particularly during the pre-Delta and Delta periods. Among patient catagorized moderate severity 27 (8.6%) cases were asymptomatic.

The chest radiographs exhibited abnormal presentations, with interstitial infiltration being more prevalent than patchy opacity or ground glass appearance. These results were not correlated with those of previous studies such as Anugularuengkitt S, et al, Caro-Dominguez P, et al, and Oterino Serrano C, et al[6,15,19], which identified the most common radiological presentations as peribronchovascular marking and ground glass opacity. This discrepancy may be attributed to the implementation of routine chest radiography screening in nearly all patients with SARS-CoV-2 infection, regardless of symptoms. Based on the pathophysiology of SARS-CoV-2-induced

pneumonia, early inflammation and damage typically occur within the pulmonary interstitium. This may explain the early radiographic manifestation of interstitial infiltration even in asymptomatic individuals.

Over 70% of pre-Delta and Delta variant cases were exposed through household contact, but in the Omicron variant, only half of the cases were exposed through household contact, with the other half exposed in the community or through unknown sources. This may be caused by the epidemiology of the COVID-19 Omicron variant disease that quickly spreads in the community.

The hospitalization may have been influenced by government policies implemented to manage the disease during different periods. The patients who had asymptomatic infection or mild severity were admitted to field hospitals, community isolation, or home isolation, while the patients who had moderate to severe severity were admitted to a ward or PICU. In the Omicron period, the SARS-CoV-2 virus appeared more transmissible. As the disease spread widely, the government imposed limits on the number of patients admitted to hospitals. Consequently, field hospitals, community isolation, and home isolation were established. The home isolation program, which included follow-ups monitor symptoms via telemedicine, was implemented in May 2021. In contrast, the self-isolation program, which did not include follow-ups, was introduced in March 2022. As a result, during the Delta period, many patients were admitted to home isolation more frequently than in other periods. Conversely, during the Omicron period, fewer patients were admitted to home isolation because self-isolation protocols had been established. Even if the number of patients in each period was equal, we collected the data over a short duration during the Omicron variants, so there were limitations in admission sites.

Antiviral agents were administered in 83.3% of all patients. During the pre-Delta period, favipiravir was prescribed in 74.6% of cases, which was significantly lower compared to other periods. Otherwise the Delta and Omicron periods, favipiravir became more readily accessible and sufficiently supplied within the healthcare system. This increased availability likely resulted in a higher proportion of patients receiving antiviral treatment compared to the pre-Delta period. Such improved access to antiviral therapy may have contributed to a reduction in the proportion of patients presenting with moderate severity during the Delta and Omicron periods, relative to the pre-Delta period.

The strength of this study is that we enrolled a large sample size and obtained complete data records for pediatric patients with SARS-CoV-2 infection upon their initial visit. Additionally, chest radiography was performed in almost all patients and interpreted by a radiologist. This increased the accuracy in detecting severity, resulting in a higher percentage of moderate severity compared to other studies.

Limitations of this study include the fact that the determination of variant strains in our study relied on nationwide surveillance data from the DDC MoPH Thailand to identify the predominant strains during each period; therefore, the results comparing between the periods may be inaccurate.

Furthermore, the government policies and supply availability may have influenced clinical outcomes, including hospitalization and disease control (such as antiviral medication administration, admission site, and vaccination).

Conclusions

Respiratory symptoms are the most common presentation in pediatric SARS-CoV-2 infection, consistent with previous reports. However, each period exhibits different predominant symptoms. We found fever, nausea/vomiting, and seizures, which predominated in the Omicron period, while anosmia and loss of taste predominated in the Delta period. We found that some patients had no symptoms, but they did have abnormal chest radiography. Thus, the patients in this group should receive close monitoring. However, overall, the patients achieved full recovery.

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Conflicts of Interest

The authors declare no conflict of interest.

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