Original Article

Incidence, Clinical Features, and Factors Associated with Pediatric COVID-19 Pneumonia

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Background: In December 2019, the outbreak of SARS-CoV-2 infection was first reported in Wuhan, China. It rapidly spread worldwide, causing health, economic, and social problems. In terms of health issues, the critical condition is respiratory tract infection, especially pneumonia and subsequent respiratory failure. However, the incidence and related factors of COVID-19 pneumonia among children are still not well understood.

Objective: To find the incidence and factors associated with pediatric COVID-19 pneumonia.

Materials and Methods: A cross-sectional study was performed by including patients less than 15 years old whose nasopharyngeal PCR swabs were positive for COVID-19. All patients were admitted to the cohort ward or pediatric department at ChumPhae Hospital, Khon Kaen, Thailand between January 1 and December 31, 2021. Demographic data, clinical manifestations, laboratory data, and chest radiographs reported by radiologists were collected. Descriptive statistics was performed followed by simple and multiple logistic regressions to determine the associated factors of COVID-19 pneumonia.

Results: Two hundred eighty-seven cases were included, with 114 cases or 39.7% (95% CI 34.1 to 45.7%) of abnormal chest radiographs reported. The risks associated with increasing pneumonia were weight-for-height percentage (adjusted OR 1.01, 95% CI 1 to 1.02). Aged younger than 1 year group and aged 1 to younger than 3 years old group had significantly higher risk of pneumonia than patients aged 7 to younger than 15 years old group [(adjusted OR 3.82, 95% CI 1.28 to 11.45) and (adjusted OR 5.7, 95% CI 2.62 to 12.43), respectively]. In contrast, rhinorrhea was slightly associated with lower risk (adjusted OR 0.51, 95% CI 0.3 to 0.87).

Conclusion: Among children, COVID-19 pneumonia is frequent, and the risk was increased for those in the group of less than 3 years old and having increased body weight. Rhinorrhea was slightly associated with a lower risk. Physicians and care teams should consider these factors when treating this group of pediatric patients.

Keywords: Pneumonia; COVID-19; Children; Pediatric

Since December 2019, there has been an outbreak of acute lower respiratory tract symptoms caused by an unknown organism that first developed in Wuhan, China. In January 2020, the organism was known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The outbreak later spread throughout the world. Many people have since been infected and suffered from pneumonia. Therefore, the ability to identify the risks for pneumonia and prevent viral progression before developing pneumonia may assist in decreasing the worst clinical outcomes.

According to a recent meta-analysis that collected data in China, Malaysia, Spain, Italy, and the USA, it was reported that the most common clinical symptoms for COVID-19 infected pediatrics were fever and cough, and 16% were asymptomatic[1].

A systematic review of the demographic, clinical, laboratory, and imaging features among pediatric patients in China by Cu et al[2] showed that 56.5% had inflammatory lesions of the lungs, based on computed tomography of the chest. Furthermore, pulmonary imaging data from 294 cases showed that 87 or 29.6% of the cases with ground-glass opacities, 60 or 20.4% of the cases with a local patchy shadow, 43 or 14.6% of the cases with a bilateral patchy shadow, and two or 0.7% of the cases with interstitial lesions[2]. From

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the present study, 65% of COVID-19 infected children had abnormal chest radiography. Another study by Bai et al[3]. reported that the incidence rate of pneumonia was 60.7%.

From the fifth issue of statement of the COVID-19 situation in Thai children on 29 August 2021, it was announced that the number of infected children was increasing rapidly. Some patients had high clinical severity that ended in mortality[4].

Infected pediatric clinical symptoms differ from adults, with about 5% to 6% being severe. Pneumonia was the most frequent indication for admission to the pediatric intensive care unit (PICU). According to the study of 'Risk factors associated with SARS-CoV-2 pneumonia in the pediatric population[5] in Mexico, it was found that the risk factors for COVID-19 pneumonia were age less than one year old, obesity, and comorbidity of diabetes mellitus.

Data concerning pneumonia and the clinical characteristics of COVID-19 infected children in Thailand remain scarce. Therefore, the present study aimed to examine the incidence and risk factors for COVID-19 pneumonia among this group of patients.

Materials and Methods

A cross-sectional study was performed, and data were collected from patients admitted between January first and December thirty-first, 2021, to the Pediatric Department, Cohort Ward at ChumPhae Hospital, Khon Kaen, Thailand. All pediatric patients aged less than 15 years old whose nasopharyngeal PCR swabs were positive for COVID-19 were included. The present study divided the patients into four groups, aged less than 1 year, aged between 1 and less than 3 years old, aged between 3 and 7 years old, and aged between 7 and 15 years old. In addition, in each group, they were classified in diagnosed pneumonia and non-pneumonia subgroups. Pneumonia was diagnosed by clinical presentation of respiratory distress and official chest radiograph reported by radiologist that showed abnormal lesions as interstitial infiltration, patchy infiltration/ground glass opacity (GGO), or both of interstitial infiltration and patchy infiltration/GGOs. Patients who had co-bacterial infection during treatment for COVID-19 infection, patients with primary condition involved with bacterial infection but coincidentally found COVID-19 infection, or patient with condition of acute appendicitis, septic shock with blood culture positive for bacteria, urinary tract infection, and complication as thrombophlebitis were excluded.

Calculation of sample size for logistic regression[6]

by assuming one interested factor can explained variance equal to 40% and adjusting in case of multiple independent variables explained the variance $R^2=0.6$. By using odds ratio from the study of Moreno-Noguez et al (2020)[5], the sample size required was 100. However, data were collected throughout the year to cover all possible clinical characteristics.

The present study was approved by the ChumPhae Hospital Research Ethics Committee (EC number HE 641013).

In the present study, 287 cases of children with COVID-19 were included. Baseline characteristics including age, gender, risk of underlying disease, weight, and height were collected. The authors calculated weight-for-height percentage, then classified into normal, overweight, obesity, and morbid obesity[7]. In contrast with malnutrition classified by weight-for-height percentage, weight-for-age percentage used the Gomez and Waterlow classification[8].

Clinical symptoms such as fever, dry cough, productive cough, rhinorrhea, anosmia-hyposmia, desaturation, differential saturation between pre-/post-exercise, headache, drowsiness, cyanosis, diarrhea, vomiting, abdominal discomfort, rash, conjunctivitis, sore throat, and loss of taste were collected.

Desaturation was SpO_2 less than 95% in case of no underlying disease of congenital cyanotic heart, or SpO_2 decrease from the baseline in case of congenital cyanotic heart diseases. Differential SpO_2 explained by decreased SpO_2 at least 3% after exercise by sit-to-stand test for exercise induced desaturation in COVID-19 patients: sit down then stand up 20 to 30 times/minute for one minute. Limitation in young children that cannot obeyed command, used of average SpO_2 that was measured at least two times in one day less than 95% meant desaturation.

Laboratory data included white blood cell count, absolute lymphocyte count, and platelet count, which were collected and classified as leukopenia, leukocytosis, lymphopenia, lymphocytosis, thrombocytopenia, thrombocytosis, or normal by the age-specific blood cell indices range from The Harriet Lane Handbook of Pediatrics[9].

Chest radiography was performed in all cases and officially reported by qualified radiologists to diagnose normal, interstitial pneumonia, or ground-glass opacity pneumonia.

Baseline characteristics were calculated using descriptive statistics, frequencies with percentages for categorical variables, median and interquartile range (IQR) for continuous variables. Shapiro-Wilk test was

performed to check the normality of all continuous variables. Incidence of COVID-19 pneumonia among children and 95% confidence interval (CI) was calculated. Simple logistic regression was performed to crudely explore the association between pneumonia and each independent variable including demographic data, clinical data, and laboratory data. The independent variables which had p-value of likelihood-ratio test from simple logistic regression less than 0.2 were included in an initial model for multiple logistic regression analysis. The multiple logistic regression with backward elimination method were conducted to identify the final model. Crude odds ratio (OR) and adjusted OR with its 95% CI were calculated using simple and multiple logistic regressions. All statistical analyses were preformed using R program language and "epiDisplay" package on RStudio[10-12].

Results

In the 287 children aged less than 15 years old whose nasopharyngeal PCR swabs were positive for COVID-19, the official radiographic report found 114 cases or 39.7% (95% CI 34.1 to 45.7%) had pneumonia. No severe pneumonia was collected, only one case of pneumonia with acute asthmatic attack impending respiratory failure, which used humidified high flow nasal cannula was transferred to the tertiary center.

Characteristics of COVID-19 in children

Demographic characteristics data: From 287 cases, the median age was 7.35 years (IQR 3.77, 10.87). The median age of the patients classified as the pneumonia group was 5 years (IQR 1.9, 10.9). This compared with the non-pneumonia group, which median age was 7.9 years (IQR 5.3, 10.5). Thirteen cases or 11.4% in the age group less than 1 year old, 29 cases or 25.4% in the group aged between 1 to below 3 years old, 23 cases or 20.2% in the group aged 3 to below 7 years old, and 49 cases or 43% in the group aged 7 to below 15 years old had pneumonia, as shown in Table 1.

Gender data showed the proportion of males to females was 149 cases or 51.9% to 138 cases or 48.1%, respectively. Classified as the pneumonia group, male gender comprised 61 cases or 53.5% and female gender comprised 53 cases or 46.5%.

The median weight-for-height percentage was 103 (IQR 90, 125) for the pneumonia group and 100 (IQR 87.8, 116.5) for the non-pneumonia group. For the majority, the nutritional status was normal. There

Table 1. Baseline characteristics and clinical features in COVID-19 infected pediatrics

Variable	No pneumonia (n=173); n (%)	Pneumonia (n=114); n (%)	p-value
Age (years)			<0.01
Less than 1	6 (3.5)	13 (11.4)	
1 to less than 3	14 (8.1)	29 (25.4)	
3 to less than 7	53 (30.6)	23 (20.2)	
7 to less than 15	100 (57.8)	49 (43.0)	
Median (IQR)	7.9 (5.3,10.5)	5 (1.9,10.9)	0.001*
Sex (male)	88 (50.9)	61 (53.5)	0.66
Weight-for-height percentage; median (IQR)	100 (87.8,116.5)	103 (90,125)	0.109*
Obesity			0.35
Normal	114 (69.5)	63 (57.8)	
Over weight	33 (20.1)	30 (27.5)	
Obesity	15 (9.1)	12 (11.0)	
Morbid obesity	2 (1.2)	4 (3.7)	
Malnutrition	45 (26)	26 (22.8)	0.54
Underlying disease	1 (0.6)	2 (1.8)	0.34
Asymptomatic	29 (16.8)	15 (13.2)	0.38
Symptomatic	144 (83.2)	99 (86.8)	0.41
Fever	95 (54.9)	65 (57.0)	0.73
Dry cough	93 (53.8)	60 (52.6)	0.85
Productive cough	26 (15)	12 (10.5)	0.27
Rhinorrhea	78 (45.1)	38 (33.3)	0.05
Anosmia or hyposmia	14 (8.1)	11 (9.6)	0.65
Desaturation or differential saturation pre-/post-exercise more than 3%	0 (0.0)	1 (0.9)	0.22
Headache	16 (9.2)	8 (7.0)	0.5
Drowsiness	0 (0.0)	3 (2.6)	0.03
Cyanosis	0 (0.0)	1 (0.9)	0.22
Tachycardia	14 (8.1)	13 (11.4)	0.35
Diarrhea	5 (2.9)	7 (6.1)	0.18
Vomiting	4 (2.3)	2 (1.8)	0.75
Abdominal	0 (0.0)	0 (0.0)	NA
Rash	3 (1.7)	6 (5.3)	0.09
Conjunctivitis	2 (1.2)	1 (0.9)	0.82
Tasteless	5 (2.9)	3 (2.6)	0.90
Sore Throat	23 (13.3)	15 (13.2)	0.97

IQR=interquartile range

* Calculated by Mann-Whitney U test

were increases in the percentages of overweight, obesity, and morbid obesity in the pneumonia group when compared with the non-pneumonia group. On the contrary, malnutrition was found to be 22.8% in the pneumonia group and 26% in the non-pneumonia group.

The risks for underlying diseases including diabetes mellitus, congenital heart diseases, chronic

lung disease, asthma, hematologic malignancy, cirrhosis, and chronic kidney disease were summed up in one factor. There was one case of Tetralogy of Fallot and valvular heart disease in the pneumonia group or 1.8%, and one case of asthma in the-non pneumonia group or 0.6%.

Clinical features: Clinical symptoms between the pneumonia and the non-pneumonia groups were not significantly different. Fever was the most frequent symptom in both groups, with 65 cases or 57% and 95 cases or 54.9%, respectively. The second and third most common symptoms were dry cough and rhinorrhea, respectively, as shown in Table 1.

The least common clinical symptoms were abdominal discomfort, desaturation, and differential oxygen saturation between pre-/post-exercise periods. Cyanosis occurred in one case diagnosed as COVID-19 pneumonia with Tetralogy of Fallot.

Laboratory findings: For the 287 cases included in the present study, laboratory data for nine cases were missing. From 279 cases classified, 111 cases were pneumonia, and 167 cases were non-pneumonia. The results of complete blood count were collected from ChumPhae Hospital or from a community hospital. The results were identified as leukopenia, leukocytosis, lymphopenia, lymphocytosis, thrombocytopenia, and thrombocytosis by using the normal range from the Harriet Lane Handbook of Pediatrics(8). All white blood cell, lymphocyte and platelet data were not different for both groups, as shown in Table 2.

In the present study, serum biomarker, which indicated inflammation such as C-reactive protein or pro-calcitonin were scarcely performed because these tests were unavailable and increased nursing workload. Whereas viral panel antigen was not available in ChumPhae Hospital.

Chest radiograph findings included both first and second time reported, found that 114 cases had abnormal chest radiograph. Chest X-ray of 69 cases or 60.53% shown patchy infiltration or GGO, whereas interstitial infiltration was found in 21 cases or 18.42%. For both interstitial and patchy infiltration found/GGO in 24 cases or 21.05%, as shown in Table 2.

Factors associated with pneumonia in pediatric COVID-19 infection

The crude analyses were performed for evaluating the association between the interested variables and pneumonia using simple logistic regressions. The present study found that age group 1, the younger than

Table 2. Summarizing of laboratory and chest radiograph report findings

Laboratory findings	Pneumonia (n=111); n (%)	Non-pneumonia (n=167); n (%)	p-value
White blood cell count			
Leukocytosis	3 (2.7)	3 (1.8)	0.61
Leukocytopenia	10 (9.0)	14 (8.4)	0.86
Normal	98 (88.3)	150 (89.8)	0.68
Lymphocyte count			
Lymphocytosis	2 (1.8)	3 (1.8)	1.00
Lymphopenia	13 (11.7)	17 (10.2)	0.69
Normal	96 (86.5)	147 (88.0)	0.70
Platelet count			
Thrombocytosis	24 (21.6)	33 (19.8)	0.25
Thrombocytopenia	0 (0.0)	2 (1.2)	0.71
Normal	87 (78.4)	132 (79.0)	0.89
Official chest radiograph findings in pneumonia group		n=114; n (%)	
Patchy infiltration/GGO		69 (60.53)	
Interstitial infiltration		21 (18.42)	
Both interstitial infiltration and patchy infiltration/GGO		24 (21.05)	

GGO=ground glass opacity

one year old group, was associated with an increased risk of pneumonia when compared with age group 4, the between 7 to younger than 15 years old group (OR 4.42, 95% CI 1.59 to 12.34) and age group 2, the between 1 to younger than 3 years old group, to age group 4 (OR 4.23, 95% CI 2.05 to 8.72) (Table 3).

From the crude analysis, the clinical symptom that was found to decrease the risk of pneumonia was rhinorrhea (OR 0.61, 95% CI 0.37 to 1) (Table 3).

When analyzed using multiple logistic regression, it was found that being younger than 1 year old and aged between 1 to younger than 3 years old significantly increased the risk for pneumonia when compared to those aged between 7 to younger than 15 years old (adjusted OR 3.82, 95% CI 1.28 to 11.45) and (adjusted OR 5.7, 95% CI 2.62 to 12.43), respectively. Weight-for-height percentage was also a factor associated with COVID-19 (adjusted OR 1.01, 95% CI 1 to 1.02).

On the contrary, rhinorrhea significantly decreased the risk of COVID-19 pneumonia (adjusted OR 0.51, 95% CI 0.3 to 0.87), as shown in the final model, Table 4.

Discussion

The critical condition of COVID-19 was respiratory tract infection, especially pneumonia and subsequent respiratory failure. A recent systematic

Table 3. Simple logistic regression of factor associated with COVID-19 pneumonia

Variable	OR (95% CI)	p-value
Age (years)		<0.001*
Less than 1	4.42 (1.59 to 12.34)	
1 to less than 3	4.23 (2.05 to 8.72)	
3 to less than 7	0.89 (0.49 to 1.61)	
7 to less than 15	1	
Sex (male)	1.11 (0.69 to 1.79)	0.661
Weight-for-height percentage	1.0068 (0.9991 to 1.0146)	0.083*
Malnutrition	0.84 (0.48 to 1.46)	0.537
Asymptomatic	0.75 (0.38 to 1.48)	0.403
Fever	1.09 (0.68 to 1.75)	0.725
Dry cough or productive cough	0.98 (0.61 to 1.58)	0.932
Rhinorrhea	0.61 (0.37 to 1)	0.046*
Anosmia	1.21 (0.53 to 2.78)	0.649
Desaturation or differential saturation pre-/post-exercise more than 3%	NA	NA
Tachycardia	1.46 (0.66 to 3.24)	0.351
Headache or drowsiness	0.94 (0.41 to 2.16)	0.89
Gastrointestinal (diarrhea, vomiting, abdominal pain)	1.56 (0.6 to 4.06)	0.362
Other symptoms (cyanosis or rash or conjunctivitis or tasteless or underlying disease)	1.73 (0.74 to 4.07)	0.208
Abnormal white blood cell count	1.17 (0.54 to 2.52)	0.688
Abnormal lymphocyte count	1.15 (0.56 to 2.35)	0.706
Abnormal platelet count	1.04 (0.58 to 1.87)	0.895

OR=odds ratio; CI=confidence interval; NA=not applicable

* p<0.2, were included in the initial model

Table 4. Predictive factors associated with COVID-19 pneumonia in children

Variable	Final model	
	Adjusted OR (95%CI)	p-value
Age (years)		<0.001
Less than 1	3.82 (1.28 to 11.45)	
1 to less than 3	5.7 (2.62 to 12.43)	
3 to less than 7	1.23 (0.64 to 2.35)	
7 to less than 15	1	
Weight-for-height percentage	1.01 (1 to 1.02)	0.012
Rhinorrhea	0.51 (0.3 to 0.87)	0.013

OR=odds ratio; CI=confidence interval

review by Cu et al[2]. showed from computed tomography of the chest that 56.5% had inflammatory lesions of the lungs. Furthermore, pulmonary imaging data from 294 cases showed 87 or 29.6% of the cases with ground-glass opacities, 60 or 20.4% of the cases with a local patchy shadow, 43 or 14.6% of the cases with a bilateral patchy shadow, and two or 0.7% of the cases with interstitial lesions[2]. Another study from China also reported the incidence rate of COVID-19 pneumonia at 60.7%[3].

When compared with the present study, the authors found 114/287 cases (39.7%) had abnormal chest radiography. They were mainly in patchy infiltration/GGO, a lower incidence than the two studies from China. The difference could be from diagnosis from chest X-ray compared with chest computer tomography, races, serotype of virus, and time of study as early studies may not have adequate data for virus, transmission route, prevention, and antiviral therapy.

In Thailand, a retrospective cohort study was done in 2019 by Arayapong[13]. From 274 cases, only 45 cases or 16.4% had moderate or severe disease with abnormal chest X-ray. The present study had lower incidence of pneumonia compared with the present study at 39.7%, which may be from the underestimation of pneumonia caused by variation in reporting.

The predictive risk factors associated with COVID-19 pneumonia in children, from a study by Moreno-Noguez et al[5], were found to include age younger than one year old (OR 5.83, 95% CI 3.56 to 9.54) and children aged 1 to 3 years old (OR 2.64, 95% CI 1.72 to 4.06), diabetes (OR 12.61, 95% CI 4.62 to 34.41), obesity or diabetes (OR 2.94, 95% CI 1.75 to 4.95), which was similar to the present study. It was found that weight-for-height percentage and age younger than 3 years old were increased risk factors for COVID-19 pneumonia, in agreement with the Thai COVID-19 guideline management[14] that suggested medication and treatment for all children younger than one year old. Compared with the study by Arayapong[13], Thailand found that the factors associated with moderate to severe disease were co-morbidity (adjusted OR 18.31, 95% CI 3.9 to 81.13, p=0.001) and fever (adjusted OR 4.51, 95% CI 1.82 to 11.16, p<0.001). Conversely, the present study found that the risks of underlying diseases were not statistically significant in terms of difference because few cases had significant underlying diseases and was not similar with Arayapong[13] study with two cases in pneumonia group and one case in non-pneumonia group.

One clinical risk factor that lowered the risk of COVID-19 pneumonia was rhinorrhea. From research in Saudi Arabia by Hijazi et al[15], they found that the most frequently reported otolaryngology symptoms were sore throat at 17.3% and rhinorrhea at 14.4%. However, they did not mention the association

between rhinorrhea and COVID-19 pneumonia. No recent study described this association. Perhaps rhinorrhea is always present in upper respiratory tract infection, which differs from pneumonia, which is lower respiratory tract infection.

A recent study in Turkey by Böncüoğlu et al[16] found that serum CRP was not a significant variable of pulmonary involvement in pediatric COVID-19 infection (OR 1.389, 95% CI 0.258 to 7.486). However, serum inflammatory markers were mostly unavailable in the present study.

Limitations of the present study were 1) unavailable laboratory service thus, other significant variables may not be included such as the viral genotype, serologic study, and various serum biomarkers such as CRP and pro-calcitonin that would increase the explainable risk factors of pneumonia. 2) Some symptoms may be difficult to determine in young children so that the objective measures such as temperature and oxygen saturation would be more valid. 3) The incidence rates of pneumonia will be different in the future studies due to the availability and accessibility of COVID-19 vaccines, as well as the evolution of the virus itself from a pandemic to an endemic disease.

To accurately relate between other clinical symptoms, the underlying risk factors may require further study to explain this correlation using a larger sample size, multicenter trial, or prospective study.

The study of pediatric patients requires data from the informants and caregivers, who may not recognize the symptoms before admission. Thus, the data concerning clinical symptoms may be inaccurate. The present study had distinctive points including 1) chest radiography reported from a qualified radiologist, and 2) all cases of pediatric COVID-19 prospectively were included to assure the adequacy of data.

Conclusion

The present study found the incidence of COVID-19 pneumonia was 39.7% (95% CI 34.1 to 45.7%) among pediatric patients. The risks associated with pneumonia included weight-for-height percentage, aged younger than 3 years. In contrast, rhinorrhea exhibited lower risk for pneumonia. Young children appear to face a higher risk for developing COVID-19 pneumonia compared to older age groups, which may prompt early antiviral therapy in these age groups. For young patients who are overweight or obese, attention should be given for clinical changes and repeated chest radiographs to watch for early diagnosis of pneumonia.

What is already known on this topic?

From the recent studies in foreign countries, the results are already known that incidences of COVID-19 pneumonia in children were different, and factors associated with pneumonia were age younger than 3 years old and obesity.

What this study adds?

The incidence of pediatric COVID-19 pneumonia was 39.7%. Increased weight for height and age younger than 3 years old associated with increasing pneumonia in pediatric COVID-19 infection. The additional finding was that rhinorrhea associated with lower risk of pneumonia.

Conflicts of interest

The authors have no conflict of interest to declare.

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