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

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Abstract

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.

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 from 1st January 2021 to 31th December 2021. Demographic data, clinical manifestations, laboratory data and chest radiograph 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: A total of 287 cases were included, with 114 cases (39.7%, 95% CI 34.1 to 45.7%) of abnormal chest radiograph reported. The risks associated with increasing pneumonia were weight-for-height percentage (adjusted OR, 1.01, 95%CI; 1 to 1.02). Age < 1 year group and age 1 to below 3 years old group have significantly higher the risk of pneumonia than patients age 7 to below 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 associated with a 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 who were less than 3 years old and had increased weight. Rhinorrhea was associated with a lower risk. These factors should be taken into account by physicians and care teams while treating this group of pediatric patients.

Keywords: pneumonia, COVID-19, children, pediatric

Background

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. Subsequently, the organism was known as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in January 2020. The outbreak later spread throughout the world. Many people have since been infected with 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 56.5% had inflammatory lesions of the lungs, based on computed tomography of the chest. Furthermore, pulmonary imaging data from 294 cases showed 87 (29.6%) cases with ground- glass opacities, 60 (20.4%) cases with a local patchy shadow, 43 (14.6%) cases with a bilateral patchy shadow, and 2 (0.7%) cases with interstitial lesions.[2] From this 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 Statement of the COVID-19 Situation in Thai Children (5th issue) 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 5-6 % being severe. Pneumonia was the most frequent indication for admission to the PICU, ventilator use and subsequent death. 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 1 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, this study aimed to examine the incidence and risk factors for COVID-19 pneumonia among this group of patients.

Methods

A cross-sectional study was performed and data were collected from patients admitted to the pediatric department, Cohort Ward at ChumPhae Hospital, Khon Kaen, Thailand from 1 January 2021 to 31 December 2021. All pediatric patients aged less than 15 years old whose nasopharyngeal PCR swabs were positive for COVID-19 were included. This study divided the patients into 4 groups: aged less than 1 year, aged between 1 to less than 3 years old, aged between 3 and 7 years old, and aged between 7 and 15 years old.

Patients who had co-bacterial infection during treatment for COVID-19 infection were excluded.

The study was approved by the ChumPhae Hospital Research Ethics Committee.

In this study, 287 cases of children with COVID-19 were included. Baseline characteristics including age, sex, risk of underlying disease, weight, and height were collected. We calculated weight-for-height percentage, then classified into normal, overweight, obesity and morbid obesity.[6] In contrast with malnutrition classified by weight-for-height percentage, weight-for-age percentage used the Gomez and Waterlow classification.[7]

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.

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.[8]

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.[9,10,11]

Results

According to all 287 children aged less than 15 years old whose nasopharyngeal PCR swabs were positive for COVID-19, the official radiographic report found 114 cases (39.7%, 95% CI 34.1 to 45.7%) had pneumonia.

Characteristics of COVID-19 in children

- Demographic characteristics data

From 287 cases, the median age= 7.35 years (IQR= 3.77, 10.87), classified as the pneumonia group median age= 5 years (IQR= 1.9, 10.9) compared with the non-pneumonia group median age= 7.9 years (IQR=

5.3, 10.5). In the age group less than 1 year old, 13 cases (11.4%) had pneumonia, while 29 cases (25.4%) in the group aged between 1 to below 3 years old had pneumonia, 23 cases (20.2%) in the group aged 3 to below 7 years old had pneumonia, and 49 cases (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 (51.9%) to 138 cases (48.1%), respectively. Classified as the pneumonia group, male gender comprised 61 cases (53.5%) and female gender comprised 53 cases (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 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 (1.8%), and one case of asthma in the-non pneumonia group (0.6%).

- Clinical features

Clinical symptoms between the pneumonia and non-pneumonia groups were not significantly different. Fever was the most frequent symptom in both groups, with 65 cases (57%) and 95 cases (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. This case received systemic corticosteroid therapy to reduce the inflammatory process. Thereafter, desaturation was improved to baseline oxygen saturation values.

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

Variable	No Pneumonia (n = 173) (60.3%)	Pneumonia (n = 114) (39.7%)
Age (years): 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)
Median (IQR)	7.9 (5.3,10.5)	5 (1.9,10.9)
Gender (Male)	88 (50.9)	61 (53.5)
Weight-for-height percentage; median (IQR)	100 (87.8,116.5)	103 (90,125)
Obesity: Normal	114 (69.5)	63 (57.8)
Over weight	33 (20.1)	30 (27.5)
Obesity	15 (9.1)	12 (11)
Morbid obesity	2 (1.2)	4 (3.7)
Malnutrition	45 (26)	26 (22.8)
Underlying disease	1 (0.6)	2 (1.8)
Asymptomatic	29 (16.8)	15 (13.2)
Symptomatic	144 (83.2)	99 (86.8)
Fever	95 (54.9)	65 (57)
Dry Cough	93 (53.8)	60 (52.6)
Productive Cough	26 (15)	12 (10.5)
Rhinorrhea	78 (45.1)	38 (33.3)
Anosmia or hyposmia	14 (8.1)	11 (9.6)
Desaturation or differential saturation pre-/post exercise more than 3%	0 (0)	1 (0.9)
Headache	16 (9.2)	8 (7)
Drowsiness	0 (0)	3 (2.6)
Cyanosis	0 (0)	1 (0.9)
Tachycardia	14 (8.1)	13 (11.4)
Diarrhea	5 (2.9)	7 (6.1)
Vomiting	4 (2.3)	2 (1.8)
Abdominal	0	0
Rash	3 (1.7)	6 (5.3)
Conjunctivitis	2 (1.2)	1 (0.9)
Tasteless	5 (2.9)	3 (2.6)
Sore Throat	23 (13.3)	15 (13.2)
Abnormal White blood cell count	17 (10.2)	13 (11.7)
Abnormal Lymphocyte count	20 (12)	15 (13.5)
Abnormal Platelet count	35 (21)	24 (21.6)

- **Laboratory findings**

For all 287 cases included in the study, laboratory data for 9 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.

Table 2. Summarizing of laboratory findings.

Laboratory findings	Pneumonia n=111(%)	Non-pneumonia n=167 (%)
White blood cell count		
Leukocytosis	3 (2.7)	3 (1.8)
Leukocytopenia	10 (9)	14 (8.4)
Normal	98 (88.3)	150 (89.8)
Lymphocyte count		
Lymphocytosis	2 (1.8)	3 (1.8)
Lymphopenia	13 (11.7)	17 (10.2)
Normal	96 (86.5)	147 (88)
Platelet count		
Thrombocytosis	24 (21.6)	33 (19.8)
Thrombocytopenia	0	2 (1.2)
Normal	87 (78.4)	132 (79)

Factors associated with pneumonia in pediatric COVID-19 infection

We preformed crude analyses for evaluating the association between the interested variables and pneumonia using simple logistic regressions. Our study found that age group 1 (less than 1st year) was associated with an increased risk of pneumonia when compared with age group 4 (between 7 to below 15 years old) (OR, 4.42, 95%CI; 1.59 to 12.34) and age group 2 (between 1 to below 3 years old) to age group 4 (OR, 4.23, 95%CI; 2.05 to 8.72).

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

Variable	OR (95%CI)	P-value
Age (years) less than 1 1 to less than 3 3 to less than 7 7 to less than 15	 4.42 (1.59,12.34) 4.23 (2.05,8.72) 0.89 (0.49,1.61) 1	< 0.001*
Gender (Male)	1.11 (0.69,1.79)	0.661
Weight-for-height percentage	1.0068 (0.9991,1.0146)	0.083*
Malnutrition	0.84 (0.48,1.46)	0.537
Asymptomatic	0.75 (0.38,1.48)	0.403
Fever	1.09 (0.68,1.75)	0.725
Dry cough or productive cough	0.98 (0.61,1.58)	0.932
Rhinorrhea	0.61 (0.37,1)	0.046*
Anosmia	1.21 (0.53,2.78)	0.649
Desaturation or differential saturation pre-/post exercise more than 3%	3242877.31 (0, ∞)	0.174*
Tachycardia	1.46 (0.66,3.24)	0.351
Headache or drowsiness	0.94 (0.41,2.16)	0.89
Gastrointestinal (diarrhea, vomiting, abdominal pain)	1.56 (0.6,4.06)	0.362
Other symptoms (Cyanosis or rash or conjunctivitis or tasteless or underlying disease)	1.73 (0.74,4.07)	0.208
Abnormal White blood cell count	1.17 (0.54,2.52)	0.688
Abnormal Lymphocyte count	1.15 (0.56,2.35)	0.706
Abnormal Platelet count	1.04 (0.58,1.87)	0.895

*p-value < 0.2, were included in the initial model

When analyzed using multiple logistic regression, it was found that being aged less than 1 year old and aged between 1 to below 3 years old significantly increased the risk for pneumonia when compared to those aged between 7 to below 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 final model, Table 4.

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

Variable	Initial model		Final model	
	Adjusted OR (95%CI)	P-value	Adjusted OR (95%CI)	P-value
Age (years)		< 0.001		< 0.001
less than 1	3.81 (1.27,11.4)		3.82 (1.28,11.45)	
1 to less than 3	5.67 (2.6,12.34)		5.7 (2.62,12.43)	
3 to less than 7	1.17 (0.61,2.26)		1.23 (0.64,2.35)	
7 to less than 15	1		1	
Weight-for-height percentage	1.01 (1,1.02)	0.014	1.01 (1,1.02)	0.012
Rhinorrhea	0.52 (0.3,0.89)	0.016	0.51 (0.3,0.87)	0.013
Desaturation or differential saturation pre-/post exercise more than 3%	3059108.38 (0,Inf)	0.185		

Discussion

The critical condition of COVID-19 was respiratory tract infection, especially pneumonia and subsequent respiratory failure. A recent systematic 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 (29.6%) cases with ground- glass opacities, 60 (20.4%) cases with a local patchy shadow, 43 (14.6%) cases with a bilateral patchy shadow, and 2 (0.7%) cases with interstitial lesions.[2] From this study, 65% of COVID-19 infected pediatric patients had abnormal chest radiography. Another study from China also reported the near incidence rate of COVID-19 pneumonia at 60.7%.[3]

In Thailand, a retrospective cohort study was done in 2019 by Arayapong N.[12] From 274 cases, only 45 cases (16.4 %) had moderate or severe disease with abnormal chest X-ray compared with pneumonia in our study (39.7%), which may be from the underestimation of pneumonia caused by variation in reporting.

When compared with our study, we found 114/287 cases (39.7%) had abnormal chest radiography, a lower incidence than 2 studies from China. The difference would likely be from races, serotype of virus, and time of study (early studies may not have adequate data for virus, transmission route, prevention and antiviral therapy). Our study reported a higher incidence of COVID-19 pneumonia among children than a recent study in Thailand.

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 less than 1 year old (OR, 5.83; 95%CI, 3.56-9.54) and children aged 1 to 3 years old (OR, 2.64; 95%IC, 1.72-4.06); diabetes (OR, 12.61,95%CI; 4.62-34.41); obesity and/or diabetes (OR, 2.94, 95%CI; 1.75-4.95), Similar to our study, it was found that weight-for-height percentage and age less than 3 years old were increased risk factors for COVID-19 pneumonia, in agreement with Thai COVID-19 guideline management[13] which suggested medication and treatment for all children aged less than 1 year old. Compared

with the study by Arayapong[12], 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-value 0.001) and fever (adjusted OR, 4.51, 95%CI; 1.82 to 11.16, p-value < 0.001). Conversely, our study found that the risks of underlying diseases were not statistically significant in terms of difference because the included cases had a low risk of underlying diseases (2 cases in pneumonia group and 1 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 O. Hijazi et al.[14], it was found that the most frequently reported otolaryngology symptoms were sore throat (17.3%) and rhinorrhea (14.4%). However, they did not mention the association between rhinorrhea and COVID-19 pneumonia. No recent study describes this association, perhaps rhinorrhea always present in upper respiratory tract infection differs from pneumonia which is lower respiratory tract infection.

Due to the limitations of laboratory service, other significant variables may not be included such as the viral genotype, serologic study, and various biomarkers that would increase the explainable risk factors of pneumonia. Some symptoms may be difficult to determine in young children so that the objective measures such as temperature, oxygen saturation would be more valid. The incidence rates of pneumonia will be different in 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 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. This study had distinctive points including 1) chest radiography reported from a qualified radiologist, and 2) all cases of pediatric COVID-19 prospectively included to assure the adequacy of data.

Conclusion

This study found that 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 below 3 years. In contrast, rhinorrhea exhibited a lower risk for pneumonia. Young children appear to face a higher risk for developing COVID-19 pneumonia compared to other 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.

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