Original Article

Rates of Acute Wheezing in Children During the COVID-19 Pandemic in Rayong Province, Thailand

Patcharapa Nabthuedee[1]; Korpkarn Sawatdirak[1]; Monrudee Subin1; Takdanai Sangnopparat[1]; Lakkana Thaikruea[2]



Patcharapa Nabthuedee

[1] Sri Rayong Hospital, Muang District, Rayong Province, Thailand
[2] Samui Comprehensive Maritime Safety Center, Ministry of Public Health, Surat Thani province, Thailand

*Address Correspondence to author:
Lakkana Thaikruea
Samui Comprehensive Maritime Safety Center, Koh Samui Hospital
61 Moo 1 Ang Thong sub-district, Ko Samui District, Surat Thani province, 84140, Thailand.
email: lakkana.t@cmu.ac.th

Received: April 26 ,2024
Revision received: April 29,2024
Accepted after revision: July 11 ,2024
BKK Med J 2024;20(2): 80-86.
DOI: 10.31524/bkkmedj.2024.21.005
www.bangkokmedjournal.com

Abstract

OBJECTIVES: This study investigates the rates of acute wheezing and identifies the associated risk factors among children under five during the COVID-19 pandemic in Rayong Province, Thailand.

MATERIALS AND METHODS: A retrospective study was performed on pediatric patients aged from one day to five years who were diagnosed with respiratory diseases (ICD-10 codes J00-J99) at Sri Rayong Hospital between 2019 and 2022. The study included 6,733 patients with a total of 25,830 visits. Data were retrieved from the hospital's information system.

RESULTS: From the study the majority of patients were male (51.77%). The highest acute wheezing rate appeared post-COVID-19 pandemic (25.16%) and the lowest acute wheezing rate appeared during COVID-19 pandemic (17.57%). The numbers of acute wheezing in all three phases were relevant to respiratory syncytial virus (RSV) infection. Tripledemic was not found, but only two viruses, COVID-19 and RSV were detected. In addition, no association of acute wheezing with infections of influenza A/B and COVID-19 was found, possibly because these infections rarely caused acute wheezing in children under five years old. Multiple logistic regression presented significant risk factors associated with acute wheezing, namely RSV infection (adjusted Odds ratio; 95% confidence interval (4.29; 2.34-7.86), human metapneumovirus (hMPV) infection (3.40; 1.32 - 8.74) and eosinophilia (2.51; 1.33-4.76).

CONCLUSION: Acute wheezing was highest in the post-COVID-19 pandemic (25.16%) and lowest in the period that had implemented COVID-19 preventive measures (17.57%). The infections of RSV and hMPV as well as eosinophilia were the risk factors associated with acute wheezing. The dramatic increase in RSV outbreaks after the easing of lockdown and restriction measures might be due to the immunity debt or immunity gap. COVID-19 prevention measures could only temporarily reduce RSV infection along with acute wheezing symptoms. RSV can be prevented by active immunity (monoclonal antibodies and vaccine). Infection and acute wheezing should be better prevented by RSV vaccine.

Keywords: acute wheezing, COVID-19, respiratory syncytial virus, non-pharmaceutical intervention, tripledemic, immunity debt

Acute wheezing is commonly experienced by children under five years of age. Wheezing is a continuous sound occurring on exhalation when the airway is partially blocked. Therefore, children under five years are prone to wheezing due to the small anatomy of their airways.[1] Acute wheezing may result from asthma, bronchiolitis, or lower respiratory tract infection.[2] The violence of acute wheezing is varied which may cause the child to be hospitalized or admitted to the intensive care unit and may incur medical expenditures.[3] The common viral infections that may result in acute wheezing in children include respiratory syncytial virus (RSV), rhinovirus, parainfluenza virus, human adenovirus(HAdV), human bocavirus (HBoV), human enterovirus (HEVs), human metapneumovirus (hMPV), human coronavirus (HCoVs) and Influenza.[4] The risk factors of allergic asthma that can cause wheezing include aero allergen sensitization and eosinophilia.[5]

In 2022, COVID-19 spread around the world, however, the report from the USA showed that most children experienced mild or no symptoms.[6] A study from Italy revealed that the visits of children especially with respiratory diseases to the Emergency Room decreased during the COVID-19 pandemic. On the other hand, COVID-19 resulted in some preventive measures such as hand washing, mask-wearing, online education, and quarantine of people who were at risk of infection.[7] These measures had a beneficial effect on the prevention of other respiratory diseases (such as influenza virus A, influenza virus B) and virus that cause acute wheezing in children (such as RSV, hMPV, and rhinovirus).[8]

Rosenfeld N, et al.[9] conducted a birth-cohort study to learn of the impact of the COVID-19 pandemic on respiratory morbidity in infancy. The study compared a cohort of infants born between pre-COVID-19 and COVID-19 pandemic. The study demonstrated a decrease in wheezing morbidity in infants born during the peak of the COVID-19 pandemic, compared with infants born during the preceding year (From 25.50% to 15.40%, *p* 0.003).[9] Moreover, the study showed a significant decrease in the use of bronchodilators, Emergency (ER) visits, hospitalization with lower respiratory symptoms, and the diagnosis of pneumonia in infants born during the peak of the COVID-19 pandemic, compared with infants born during the pre-COVID-19 pandemic.[9] Since the outbreak was likely a sterile period, most infants were quarantined at home so they had decreased exposure to respiratory tract infections. However, natural infection is a mechanism of the immune system in the early stages of life. Thus, an extensive study should be conducted to learn of other possible risks that appeared after COVID-19.[9]

No study had been performed in Thailand on the rate of acute wheezing among children under five years of age in the situation of the COVID-19 pandemic. Knowledge of the trend of acute wheezing during the peak of COVID-19 and post-COVID-19 pandemic was limited. Sri Rayong Hospital is a secondary private hospital with 55 beds, located in Rayong Province. It is dedicated to providing healthcare services to pediatric patients with common or specific diseases including respiratory diseases and allergies. The trend of pediatric patients admitted to Sri Rayong Hospital has increased every year. In 2021, 5.50% of children under five years old in Rayong Province had been hospitalized at Sri Rayong Hospital. In 2022, the number of pediatric patients hospitalized in Sri Rayong Hospital increased by 11.20% from 2021. During the COVID-19 pandemic, Sri Rayong Hospital revised the measures of the Acute Respiratory Infection Clinic (ARI Clinic) such as administering a COVID-19 screening by rapid test or antigen test kid (ATK test) for every pediatric patient who visited the ARI Clinic to decrease the spread of pathogens. Therefore, the study on the tendency of acute wheezing during the COVID-19 pandemic, the possible risk factors that may cause acute wheezing such as viral infection (RSV, rhinovirus, hMPV, influenza A/B, and COVID-19), and the allergic asthma risk factors that may cause such as eosinophilia is important.[5] This study aimed to determine acute wheezing rates and the risk factors for acute wheezing in pediatric patients under five years, who had been diagnosed with respiratory diseases and received treatment in Sri Rayong Hospital. The findings were useful for improving medical services with patient safety standards for pediatric patients, sharing with the concerned parents, and developing an approach to triage the severity of children with this condition.

Material and Methods

This study was a retrospective study among pediatric patients, aged one day to five years, who had been diagnosed with respiratory diseases (ICD 10 codes J00-J99) and received treatment in Sri Rayong Hospital between 2019 and 2022. The total number of pediatric patients was 12,213 and 6,736 were diagnosed with respiratory diseases (ICD 10 codes J00-J99). The secondary data were obtained from the hospital information system.

The inclusion criteria were patients with information regarding respiratory illness, the physical examination, and the bronchodilators usage.

The exclusion criteria were patients having one of the following diseases: congenital heart disease, cerebral palsy, structural airway malformation/ bronchopulmonary dysplasia, or immunodeficiency disease. Thus, three cases were excluded because of one cerebral palsy and two congenital heart diseases. The total population was 6,733 cases with 25,830 visits (Figure 1). All medical records were complete.

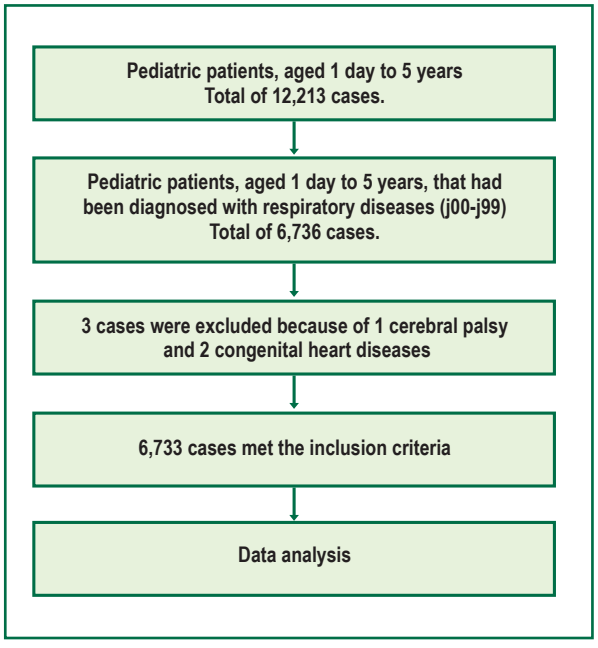


Figure 1: Flow of Case Selection

Data Collection

The secondary data for this study included demographic data (age, gender, nationality, province), respiratory illness (medical history of respiratory diseases, physical examination related to the respiratory system), laboratory (percent of eosinophils, ATK test, real-time reverse transcription polymerase chain reaction (RT-PCR), nasal swab for Influenza A/B antigen, RSV antigen, and hMPV. These secondary data were created for further analysis without identifying the individual.

Although the definition of wheezing represented by bronchospasm should be confirmed by health workers,[10] very few patients presented symptoms of wheezing when attending hospital. Parenteral report can be used for defining wheezing as reported by other studies.[11,12] Thus, acute wheezing in this study was defined as a patient who met at least two inclusion criteria from three of the following criteria: 1) A history of cough or dyspnea; 2) Health workers documented wheezing or rhonchi or secretion sound on physical examination;[13,14] 3) Salbutamol administration.

The presence of risk factors was defined as being male, at least 4% eosinophil count, viral infections (RSV, hMPV, Influenza A, and Influenza B) detected by positive viral antigen assay test, COVID-19 infection detected by positive ATK test (Rapid test with 100% specificity and 98%sensitivity) or by positive SAR-CoV2 real-time RT-PCR. Influenza test was rapid test Ag (Quick chaser influenza). Sensitivity and specificity for influenza A were 97.44% and 100% and for influenza B were 90.63% and 98.82%.[15]

The COVID-19 situation in Thailand was divided into the following phases: [16,17]

- Phase 1-Pre-COVID pandemic: The period before the COVID-19 pandemic, 1 January 2019 – 31 March 2020.
- Phase 2-COVID-19 pandemic: The measures to control the spread of COVID-19 and the lockdown had been strictly implemented. This period was between 1 April 2020 – 31 December 2021.
- Phase 3-Post-COVID-19 pandemic: Some measures were relaxed such as opening up the country and resuming onsite education. This period was between 1 January 2022 – 31 December 2022.

Data Analysis

Data were analyzed using descriptive analysis statistics including proportion (Percentage), median (Interquartile range), and mean (±Standard deviation (SD)) depending on data distribution. The relationship between acute wheezing and individual risk factors was determined using a univariate analysis including Chi-square test or mid-P exact tests that depended on expected value (< 5), and risk ratio with 95% confidence intervals (RR; 95% CI). Multivariate analysis included unconditional multiple logistic regression. The backward hierarchical selection was used to eliminate risk factors from the model at a 0.10 level of significance. An alpha level less than or equal to 0.05 was considered statistically significant.

Ethics

The study, ref. REC001/2565, had been considered and approved by the International Review Board of Bangkok Hospital Rayong (EC 001/2565) on 3 October 2022.

Results

The population of this study was 6,736 with 25,836 visits. Three of them were excluded from the study: one cerebral palsy and two congenital heart disease cases. The remaining study population was 6,733 with 25,830 visits. The majority of the population was male, 51.77%. The median age of the population in all three phases of the COVID-19 pandemic in Thailand was likely similar. The first phase was 2.50 years (1.30 – 3.80), the second phase was 2.40 years (1.20 – 3.80) and the third phase was 2.90 years (1.50 – 3.90).

Trends of Acute Wheezing During the COVID-19 Pandemic

The rates of acute wheezing were significantly different (P-value < 0.01). In a sequence of COVID-19 situations, the highest prevalence appeared during post-COVID-19 and the lowest prevalence appeared during the COVID-19 pandemic (Table 1).

Acute Wheezing and Viral Infection

The numbers of acute wheezing in all three phases were relevant to RSV infection. The RSV infections in 2019 and 2020 were similar, whereas there was no incidence of RSV infection in 2021. During this period, the Thai government implemented non-pharmaceutical public health interventions. However, RSV infection and acute wheezing in 2022 had remarkably increased simultaneously, higher than those in the period between 2019 and 2020. There was no relationship between acute wheezing and both influenza and COVID-19 infection (Figure 2). The number of acute wheezing was highest after the COVID-19 pandemic. It was found that there was an increase in the number of infections with COVID-19, RSV, and influenza A/B, respectively. However, the trends of influenza A/B in all three phases were lower than in the pre-COVID-19 pandemic period (Figure 2). In 2022, schools opened for onsite learning. The COVID-19 infection rates increased but were lower than RSV infection rates. This period was RSV season in Thailand. Furthermore, the COVID-19 infection would initially affect adult and school aged children more than this study group (five years and below) (Figure 2).

Table 1: Patients with Acute Wheezing.

Phase of COVID-19 Pandemic	Total Visits	Patients with Acute Wheezing n (%)
Pre-COVID-19 Pandemic	9,795	2,292 (23.40)
COVID-19 Pandemic	6,860	1,205 (17.57)
Post-COVID-19 Pandemic	9,175	2,308 (25.16)

* Chi-square for trend **p* value < 0.01

ISSN 2287-0237 (online)/ 2228-9674 (print)

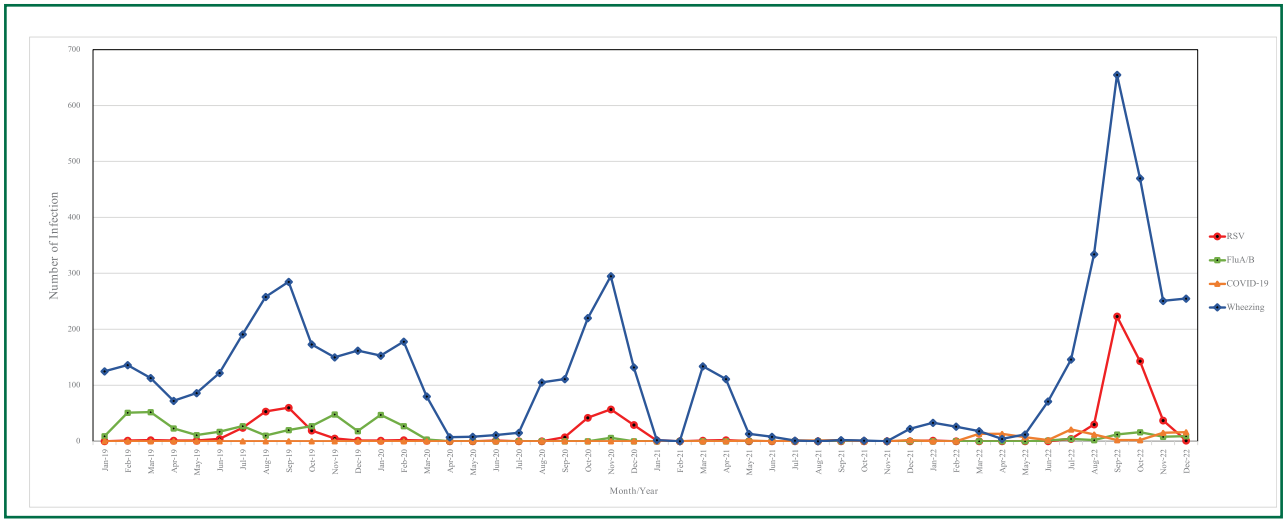


Figure 2: Numbers of the Acute Wheezing and the Infections of COVID-19, Influenza A/B and RSV by Phase of COVID-19 Pandemic.

Risk Factors Associated with Acute Wheezing

The univariate analysis showed the risk factors that are significantly related to acute wheezing. Acute wheezing in male patients was 1.12 times higher than in female patients. Acute wheezing in patients with eosinophilia was 1.51 times higher than in other patients (Table 2). For viral infections, acute wheezing in patients with an infection of RSV or hMPV was 1.58 times higher than in patients without an infection of RSV or hMPV (Table 2).

Based on unconditional multiple logistic regression, risk factors associated with acute wheezing statistically significant were patients with eosinophilia (2.51; 1.33 - 4.76), patients with RSV infection (4.29; 2.34 - 7.86) and patients with hMPV infection (3.40; 1.32 - 8.74) (Table 3).

Table 2: Risk Factors Associated with Acute Wheezing Based on Univariate Analysis. Univariate Analysis.

Risk Factors	With Acute Wheezing n (%)	Without Acute Wheezing n (%)	Relative Risk (95% CI)
Gender			
Male	3,304 (23.67)	10,657 (76.33)	1.12 (1.07-1.18)*
Female	2,501 (21.07)	9,368 (78.93)	
Eosinophilia			
Yes	242 (60.96)	155 (39.04)	1.51 (1.38-1.65)*
No	1,414 (40.45)	2,082 (59.55)	
Respiratory Syncytial Virus			
Yes	515 (66.58)	257 (33.42)	1.58 (1.47-1.69)*
No	1,061 (33.29)	1,477 (66.71)	
Human metapneumovirus (hMPV)			
Yes	34 (77.27)	10 (22.73)	1.58 (1.32-1.89)*
No	288 (49.05)	299 (50.95)	

**p value < 0.01

Table 3: Risk Factors Associated with Acute Wheezing Based on Unconditional Multiple Logistic Regression Analysis*

Risk Factors	Adjusted Odds ratio	95%CI	p value
hMPV			
Yes	3.40	1.32 - 8.74	0.011
Respiratory Syncytial Virus			
Yes	4.29	2.34 - 7.86	< 0.001
Eosinophilia			
Yes	2.51	1.33 - 4.76	0.005

* Backward hierarchical selection to eliminate risk factors from the model at a significance level of 0.10

Discussion

The entire population of this study was pediatric patients and excluded only three cases, which was considered very comprehensive. The acute wheezing had tentatively decreased during COVID-19 pandemic and was like the results of the study of Rosenfeld N, et al.[9] that revealed the decrease of acute wheezing during COVID-19 pandemic. In addition, the number of visits to the ARI Clinic had also decreased during the COVID-19 pandemic, similar to studies in Israel and Italy.[7,18] This study also showed that rates of infections with RSV and Influenza decreased in COVID-19 pandemic and no incidence of COVID-19. Especially, in 2019, there were very low infections with RSV, Influenza, and COVID-19 because of COVID-19 preventive measures or non-pharmaceutical interventions. It was similar to the studies conducted in China[19] and Japan[8]. Non-pharmaceutical interventions include washing hands, wearings mask, personal isolation of ill individuals, avoiding crowding, school and work place closures, traveler health advice and public health quarantine.[20] Since RSV, Influenza and COVID-19 are viruses that cause respiratory infection via droplet and contact transmission [21-23] ; therefore, wearing masks helps to restrict virus droplets from a cough or sneeze. Washing hands and cleaning immediate surroundings can prevent infection from contact transmission.[19] Moreover, influenza and COVID-19 viruses produce occasionally small particles as an airborne transmission, so that crowding avoidance and ventilation area possibly decrease rates of infection.[21,23] Thus non-pharmaceutical interventions have preventive efficacy to limit respiratory infections during the pandemic and this indirectly reduces acute wheezing caused by viral infection. Since post COVID-19 pandemic has shown a dramatic increase of acute wheezing in Sri Rayong hospital. The results of this study lead to the development of acute departments, ARI clinics and inpatients departments. Furthermore, environmental adjustments were implemented in the hospital under the infectious policy for patient safety.

This study also found that the COVID-19 pandemic had affected the nature of RSV and influenza A/B virus outbreaks in the Rayong Province. The line graph (Figure 2) demonstrated that the outbreak of the RSV virus usually occurred in the rainy to winter season every year. However, there was no RSV infection in 2021 or COVID-19 pandemic but the RSV infection in post COVID-19 pandemic was raised and remarkably higher than pre-COVID-19. Also, COVID-19 infection increased in children under five years of age when RSV and influenza A/B virus spread, which was similar to the outbreak nature in the USA and New Zealand. It was called "Tripledemic" which meant a simultaneous increase in cases of COVID-19, influenza, and RSV.[24-26] This dramatic increase in RSV infection could be explained by immunity debt or immunity gap, referring to the lockdowns weakening children's immune systems and robbing them of their natural ability to fight off viral infections. Thus, after loosening the intensive lockdown measures and the outbreak of RSV, there has been an increase in the severity of RSV-infected children.[27,28] However, only two viruses (COVID-19 and RSV) were identified in this study. The spread of the influenza virus increased less than in the pre-COVID-19 pandemic while the situation of the influenza outbreak in Thailand, reported by the Division of Epidemiology, had increased. According to Royal Thai Ministry of Public Health, rate of influenza infection in children 0-4 year was higher than other age groups between 2020 and 2022, which were 887.01, 111.84 and 496.23 per 100,000 population.[29] The data of this study showed that the influenza infection rate decreased after 2019. During July to September 2022, the rate of influenza of all ages were 1 to 10 per 100,000 population in Rayong province.[29] The possible reason was the proactive influenza vaccination program in Rayong province, which started in 2019 to the present. Adequate vaccination resulted in herd immunity. This finding led us to promote and provide influenza vaccination in the community, in schools, companies and temples. Nowadays, RSV vaccine for young children was not available. Whereas monoclonal antibody and Nirsevimab are provided only for at-risk infants.[30] Besides non-pharmaceutical interventions, breastfeeding is a primary prevention against RSV associated acute lower respiratory tract infection.[31] Thus, promotion of breastfeeding should be put forward and encouraged in nursery care and lactation clinics.

This study found that acute wheezing was significantly associated with RSV and hMPV infection. Also, RSV and hMPV were a cause of bronchiolitis and lead to wheezing.[32,33] The relationship between RSV and acute wheezing had decreased and increased in the same direction in all three phases. For data of hMPV infection, it was limited because hMPV infection only appeared in Sri Rayong Hospital in 2022, so it was not possible to detect the trend of the hMPV outbreak. Thus, the hMPV results should be interpreted carefully. This study found no association between acute wheezing and infections of influenza A/B and COVID-19. Part of the reason was that the incidence of acute wheezing in pediatric patients under five years of age with influenza virus infection was low.[34] Also, most cases of COVID-19 infection in children were asymptomatic.[35] In addition, this study showed that acute wheezing was associated with eosinophilia which was consistent with other studies because eosinophilia in children with wheezing indicated that the child was prone to allergies or asthma.[36,37] However, not all pediatric patients with wheezing required skin tests, so it not all areas of allergy risks could be indicated. Also, eosinophilia was not caused by allergies alone. It might be also caused by parasitic infections and mycoplasma bacteria.[38] The strength of this study was the representativeness of the target population and a good quality database. The findings of this study contribute to the designing of a hospital for children, improved management of wheezing and acute respiratory infection in children, and provided health education and vaccination for communities.

ISSN 2287-0237 (online)/ 2228-9674 (print)

Conclusion

Acute wheezing was highest in the post-COVID-19 pandemic (25.16%) and lowest in the period that had implemented COVID-19 preventive measures (17.57%). The infections of RSV and hMPV as well as eosinophilia were the risk factors associated with acute wheezing. Anyhow, the COVID-19 preventive measures had affected other viral outbreaks but after loosening the lockdown the viral infections had dramatically increased and resulted in a tripled epidemic (COVID-19, influenza, and RSV) in many countries. But only two viral infections (COVID-19 and RSV) occurred in this study. Ministry of Public Health does not routinely provide influenza vaccine to all provinces in Thailand. The influenza infection was not high, this might be due to the proactive influenza vaccination program in Sri Rayong Hospital. RSV can be prevented by active immunity.

Recommendation

The impact of acute wheezing in children substantially influenced to physical, mental and socioeconomic. Non-pharmaceutical intervention is effective method to reduce viral associated respiratory tract infection. COVID-19 and influenza vaccines are primary prevention that should be promote for public. In addition, children with recurrent wheezing should be monitored long term for allergic asthma.

In the long term, breastfeeding is a primary prevention against RSV-associated acute lower respiratory tract infection.[31] Breastfeeding promotion should be put forward and encouraged in nursery care and lactation clinics.

Further studies on wheezing in children under five years of age should be conducted when the RSV vaccine is widely used and long-term respiratory effects of COVID-19 in young children.

Acknowledgment

Thank you to the Hospital Director of Sri Rayong Hospital and BDMS Health Research Center for their support of this study.

References

1. Wheezing in infants. In: Kliegman RM, Geme JS, editors. Nelson textbook of Pediatrics. 21st ed. Philadelphia, *PA: Elsevier*; 2019:2217-20.
2. Inoue Y, Shimojo N. Epidemiology of virus-induced wheezing/asthma in children. *Front Microbiol.* 2013;4:391. doi: 10.3389/fmicb.2013.00391
3. Sritipsukho P, Matchimmadamrong K, Chinratanapisit S, et al. Economic burden of hospitalization with acute wheezing in preschool children: a multi-center study. *J Med Assoc Thai.* 2016;99(Suppl. 4): S239-S245.
4. Rakes PG, Arruda E, Ingram MJ, et al. Rhinovirus and respiratory syncytial virus in wheezing children requiring emergency care. *Am J Respir Crit Care Med.* 1999;159 (3):785-90. doi: 10.1164/ajrccm.159.3.9801052.
5. Castro-Rodriguez AJ, Holberg JC, Wright AL, et al. A clinical index to define risk of asthma in young children with recurrent wheezing. *Am J Respir Crit Care Med.* 2000;162 (4 Pt 1):1403-6. doi: 10.1164/ajrccm.162.4.9912111.
6. CDC COVID-19 Response Team. Coronavirus disease 2019 in children-United States, February 12-April 2, 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69(14):422-6. doi: 10.15585/mmwr.mm6914e4.
7. Matera L, Nenna R, Rizzo V, et al. SARS-CoV-2 pandemic impact on pediatric emergency rooms: A multicenter study. *Int Environ Res Public Health.* 2020;17(23):8753. doi: 10.3390/ijerph17238753.
8. Fukuda Y, Tsugawa T, Nagaoka Y, et al. Surveillance in hospitalized children with infectious diseases in Japan: Pre and post-coronavirus disease 2019. *J Infect Chemother*. 2021;27:1639-47. doi: 10.1016/j.jiac.2021.07.024.
9. Rosenfeld N, Mandelberg A, Dalal I, et al. The impact of the COVID-19 pandemic on respiratory morbidity during infancy: A birth-cohort study. *Pediatr Pulmonol.* 2022;57(4):848–56. doi: 10.1002/ppul.25822.
10. Brand PLP, Baraldi E, Bisgaard H, et al. Definition, assessment and treatment of wheezing disorders in preschool children: an evidence-based approach. *Eur Respir J*. 2008;32:1096-110. doi: 10.1183/09031936.00002108.
11. Oksel C, Granell R, Haider S, et al. Distinguishing wheezing phenotype from infancy to adolescence. A pooled analysis of five birth cohorts. *Ann Am Thorac Soc.* 2019;16(7):868-76. doi: 10.1513/AnnalsATS.201811-837OC.
12. Hendeson J, Granell R, Heron J, et al. Associations of wheezing phenotypes in the first 6 years of life with atopy, lung function and airway responsiveness in mid-childhood. *Thorax.* 2008;63(11):974-80. doi: 10.1136/thx.2007.093187.
13. Bohadana A, Lzbicki G, Kraman SS. Fundamentals of lung auscultation. *N Engl J Med.* 2014;370:744-51. doi: 10.1056/NEJMra1302901.
14. Kim Y, Hyon Y, Jung SS, et al. Respiratory sound classification for crackles, wheezes, and rhonchi in the clinical field using deep learning. *Sci Rep.* 2021;11:17186. doi: 10.1038/s41598-021-96724-7.
15. Tagawa YS, Ozawa M, Tamura D, et al. Sensitivity of influenza rapid diagnostic tests to H5N1 and 2009 pandemic H1N1viruses. *J Clin Microbiol*. 2010;48(8);2872-7. doi: 10.1128/JCM.00439-10.
16. Plans and measures for managing the situation of COVID-19 pandemic to endemic disease [Internet]. 2022. (Accessed April 22, 2565, at https://dmsic.moph.go.th/).
17. The cancellation of Declaration of an Emergency Situation in all areas of the Kingdom of Thailand. Related Regulations and Orders. 2022. (Accessed April 22, 2022, at http://www.ractchakitcha.soc.go.th/).
18. Haklai Z, Applbaum Y, Myers V, et al. The effect of the COVID-19 pandemic on non- COVID respiratory ED visit in Israel. *Am J Emerg Med.* 2022;53:215-21. doi: 10.1016/j.ajem.2022.01.005.

19. Yang Q, Xiao X, Gu X, et al. Surveillance of common respiratory during the COVID-19 pandemic demonstrates the preventive efficacy of non-pharmaceutical interventions. Int *J Infect Dis.* 2021;105:442-7. doi: 10.1016/j.ijid.2021.02.027.
20. World health organization. Responding to community of spreading COVID-19. (Accessed June 26, 2020, at https://ddc.moph.go.th/viralpneumonia/eng/file/pub_doc/LDoc5.pdf.).
21. Bridges CB, Kuehnert MJ, Hall CB. Transmission of influenza: implication for control in health care settings. *Clin Infect Dis.* 2003;37(8):1094-101. doi: 10.1086/378292.
22. Center disease of control. Respiratory syncytial virus infection. [Internet]. 2024. (Accessed June 26, 2024, at https://www.cdc.gov/rsv/causes/?CDC_AAref_Val=https://www.cdc.gov/rsv/about/transmission.html).
23. Center disease of control. COVID-19 [Internet]. 2024. (Accessed June 26, 2024, at https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/how-covid-spreads.html)
24. Tanne JH. US faces triple epidemic of flu, RSV, and covid. *BMJ.* 2022;379:o2681. doi: 10.1136/bmj.o2681.
25. New York Times. Coronavirus in the US: Latest map and case count. 2022. (Accessed November 6, 2024, at www.nytimes.com/interactive/2021/us/COVID-19-cases.html.).
26. Grant CC, Huang QS, Trenholme A, et al. What can we learn from our 2021 respiratory syncytial virus experience?. *N Z Med J.* 2021;134(1540):7-12.
27. Hatter L, Eathorne A, Hills T, et al. Respiratory syncytial virus: paying the immunity debt with interest. *Lancet Child Adolesc Health.* 2021;5(12):e44-e45. doi: 10.1016/S2352-4642(21)00333-3.
28. Cohen R, Ashman M, Taha MK, et al. Pediatric infectious disease group (GPIP) position paper on the immune debt of the COVID-19-19 pandemic in childhood, how can we fill the immunity gap? *Infect Dis Now.* 2021;51(5):418-23. doi: 10.1016/j.idnow.2021.05.004.
29. Department of Disease Control. Situation of influenza in Thailand, B.E. 2022 [Internet]. 2022. (Accessed May 4, 2023, at https://ddc.moph.go.th/doe/pagecontent.php?page=607&dept=doe).
30. Center disease of control. Vaccine and preventable disease. [Internet]. 2024. (Accessed June 26, 2024, at https://www.cdc.gov/vaccines/vpd/rsv/index.html).
31. Mineva GM, Purtill H, Dunne CP, et al. Impact of breastfeeding on the incidence and severity of respiratory syncytial virus(RSV)-associated acute lower respiratory infections in infants: a systematic review highlighting the global relevance of primary prevention. *BMJ Global Health.* 2023;8:e009693. doi: 10.1136/bmjgh-2022-009693.
32. Hall CB, Weinberg GA, Iwane MK, et al. The burden of respiratory syncytial virus infection in young children. *N Engl J Med.* 2009;360(6):588–98. doi: 10.1056/NEJMoa0804877.
33. Zhang L, Liu W, Liu D, et al. Epidemiological and clinical features of human metapneumovirus in hospitalized pediatric patients with acute respiratory illness: a cross-sectional study in Southern China, from 2013 to 2016. *BMJ Open.* 2018;8(2):e019308. doi: 10.1136/bmjopen-2017-019308.
34. Coverstone AM, Wang L, Sumino K. Beyond respiratory syncytial virus and rhinovirus in the pathogenesis and exacerbation of asthma. *Immunol Allergy Clin N Am.* 2019;39(3):391-401. doi: 10.1016/j.iac.2019.03.007.
35. Dong Y, Mo X, Hu Y, et al. Epidemiology of COVID-19-19 among children in China. *Pediatrics.* 2020;145(6):20200702. doi: 10.1542/peds.2020-0702.
36. Walsh ER, August A. Eosinophils and allergic airway disease: there is more to the story. *Trends Immunol.* 2010;31:39-44. doi: 10.1016/j.it.2009.10.001.
37. Midulla F, Nicolai A, Ferrara M, et al. Recurrent wheezing 36 months after bronchiolitis is associated with rhinovirus infections and blood eosinophilia. *Acta Paediatr.* 2014;103:1914-9. doi: 10.1111/apa.12720.
38. Kim JH, Cho TS, Moon JH, et al. Serial changes in serum eosinophil-associated mediators between atopic and non-atopic children after Mycoplasma pneumoniae pneumonia. *Allergy Asthma Immunol Res.*2014;6:428-33. doi: 10.4168/aair.2014.6.5.428.