Acute Lower Respiratory Infection Profile in Children at Tertiary Hospital Bandung: Is There a Difference Before and During COVID-19 Pandemic?

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Abstract

This study aims to analyze differences of the prevalence and characteristics of acute lower respiratory infection (ALRI) in children at tertiary hospital before and during COVID-19 pandemic. This was an observational analytic study with cross-sectional design involving pediatric patients based on the time of the study which was in I yearprepandemic (A) and I year-pandemic period (B). For period A inpatient data were retrieved from medical records and period B used pediatric ALRI registry. The ALRI characteristics were analyzed with significance if P < .05. Prevalence in periods A and B were 5.8% (534/9252) and 4.9% (409/8283), respectively. The characteristics of ALRI for clinical, comorbidities, laboratory findings (NLR, TLC), and chest radiograph showed significant differences (P < .05). ALRI as manifestation of confirmed COVID-19 were identified in 16 (4.9%) cases. Prevalence of ALRI in children during COVID-19 pandemic is lower compared to before. There are differences in the characteristics of ALRI in pediatrics.

Keywords

COVID-19, child, prevalence, respiratory tract infection, tertiary care centre

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Introduction

Acute lower respiratory infection (ALRI) is the main cause of morbidity and mortality in children in the world, it reported as the fourth leading cause of death globally and second in low-income countries.¹⁻³ Pneumonia is the most common on ALRI, the mortality rate from pneumonia in the infant group was almost twice as high as that in the group of children aged 1 to 4 years.⁴ ALRI is a large burden disease that requires treatment in adequate health facilities, so it is important for clinicians to develop and implement strategies for management to improve the quality of care and reduce mortality.5

What happened to ALRI during COVID-19 pandemic has not been widely reported. Preventive measures against ALRI transmission during the COVID-19 pandemic aim to avoid contracting the virus by carrying out health protocols. The government implements largescale social restrictions. This regulation along with increasing incidence and local spread of COVID-19 has an impacted the referral system for health facilities, including the highest referral center in West Java Province, Dr. Hasan Sadikin General Hospital Bandung. During the large-scale social restrictions period, the hospital implemented a limitation on the number of outpatient visits and other supporting services, which resulted in a decrease in the number of visits and the number of inpatients.6,7

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Methods

Study Subject and Design

This is an observational analytic study with a crosssectional design. Study subjects were children from 1 month to 18 years old. Data on pre-pandemic study subjects was collected from March 10, 2019 – March 10, 2020. Data on pandemic study subjects was collected by consecutive sampling from March 11, 2020 – March 11, 2021.

Data Collection Tools and Procedures

The data were collected from patient medical records for study subject pre-pandemic group (A) and a one-year pandemic group (B) from pediatric ALRI registry of the Respiratory Division of Pediatrics Department, Faculty of Medicine, Universitas Padjadjaran/Dr. Hasan Sadikin General Hospital Bandung. Data taken from each patients in the form of demographic, clinical, comorbidity, supporting examinations consisting of laboratory and chest X-rays, and outcome.

Data Processing and Analysis

Data were analyzed using Chi Square and Fisher Exact for demographic characteristics, clinical, laboratory, and Mann Whitney and *T*-test for laboratory and radiology characteristics. Data analysis was performed using the Statistical Package for Social Sciences (SPSS) version 26.0. The confidence interval used in this study was 95%, so the statistical analysis was considered significant if *P* value <.05.

Results

The total number of pediatric inpatient visits during the study period of March 10, 2019 to March 11, 2021 was 17535. A total of 9252 visits were in group A and 8283 visits were group B. Based on the medical record database and electronic registries, there were total 971 cases of ALRI recorded during the study periods. A total of 28 cases were excluded because the medical record files were incomplete. The analysis on the comparison of prevalence and clinical characteristics of ALRI cases was conducted on 943 cases who were group A and group B. Group B (n=409) included all cases who visited in the 1 year pandemic period and while 534 cases recorded in group A. The prevalence of ALRI before the COVID-19 pandemic was 5.8%, while during the COVID-19 pandemic the prevalence of ALRI was 4.9%.

The characteristics of the study subjects are described in Table 1. Most of the patients were male, both in group B

Table 1. Subject Characteristics.

Characteristics	Before the pandemic (n=534)	During the pandemic (n=409)	P value*
Gender			.841
Male	313 (58.6)	243 (59.4)	
Female	221 (41.4)	166 (40.6)	
Age			<.001
<i old<="" td="" year=""><td>132 (24.7)</td><td>175 (42.8)</td><td></td></i>	132 (24.7)	175 (42.8)	
I-<5 years old	277 (51.9)	106 (25.9)	
5-<10 years old	62 (11.6)	46 (11.2)	
10-18 years old	63 (11.8)	82 (20)	
Payment method			.539
Insurance (BPJS)	504 (94.4)	379 (92.7)	
Contractor	22 (4.1)	23 (5.6)	
Non-Insurance	8 (1.5)	7 (1.7)	
Referral type			<.001
Self-admission	428 (80.1)	215 (52.6)	
Referred	106 (19.9)	194 (47.4)	
Nutritional status			.010
Severe malnutrition	121 (22.7)	94 (23)	
Malnutrition	68 (12.7)	55 (13.4)	
Normal	338 (63.3)	239 (58.4)	
Overweight	3 (0.6)	14 (3.4)	
Obesity	4 (0.7)	7 (1.7)	

*Based on Chi square test.

(59.4%) and group A (58.6%). During the pandemic, most patients with ALRI were aged <1 year (42.8%), while patients in group A were mostly aged 1 to <5 years (51.9%). Both in group A and B, more than 50% of cases had good nutritional status (58.4% and 63.3%), while overweight (3.4%) and obesity (1.7%) cases were more common during the pandemic. There was no significant difference in gender between the 2 groups (P > .05), but a significant difference in terms of age and nutritional status ware observed (P < .05). More referral patients were found in group B period (47.4%) compared to group A (19.9%).

Data regarding clinical characteristics and supporting examinations in ALRI cases were presented in the form of categorical variables and analyzed with Chi-square test. The Kolmogorov-Smirnov normality test on all numerical variables resulted in a P-value <.001 which indicates that the data distribution was not normal. Therefore, the analysis of numerical variables was carried out using the Mann-Whitney nonparametric test. The differences in clinical characteristics of ALRI before and during the pandemic are depicted in Table 2.

During the study period, the forms of ALRI observed included pneumonia and bronchopneumonia. Bronchopneumonia was found in 327 cases (80%) in the group during the pandemic and 414 cases (77.5%)

Characteristics	Before the pandemic $(n = 534)$	During the pandemic $(n = 409)$	P value*
			< 001*
rever'			<.001**
Present	456 (85.4)	300 (73.3)	
Absent	78 (14.6)	109 (26.7)	
l emperature ⁺	37.8 (36-40)	37.8 (35.7-40.0)	.346**
Cough			.041*
Present	379 (71.0)	264 (64.5)	
Absent	155 (29.0)	145 (35.5)	
Shortness of breath [†]			<.001*
Present	532 (99.6)	355 (86.8)	
Absent	2 (0.4)	54 (13.2)	
Respiratory rate [‡]			
<2 month	49 (24-70)	55 (32-70)	.017**
2-<12 month	53 (32-82)	51 (24-78)	.093
12-59 month	48 (22-88)	47 (14-82)	.168
>59 month	40 (20-82)	40 (20-72)	.809
Comorbidities [†]	× ,		
CHD	319 (59.7)	21 (5.1)	<.001*
ТВС	312 (58.4)	21 (5.1)	<.001*
Immunosuppression	335 (62.7)	9 (2.2)	<.001*
Malignancy	302 (56.6)	17 (4.2)	<.001*
Asthma	277 (51.9)	(0.2)	<.001*
Diagnosis [†]			.379*
Pneumonia	120 (22.5)	82 (20.0)	
Bronchopneumonia	414 (77.5)	327 (80)	
Outcome [†]			
Discharged	418 (78.3)	317 (77.5)	.812*
Died	116 (21.7)	92 (22.5)	
Length of hospital stay [‡]	11 (1-285)	13 (1-112)	.019**

Table 2. Differences in Clinical Characteristics of ALRI Cases.

*Chi-square test.

**Mann-Whitney test.

†n (%).

CHD: Congenital Heart Disease, TBC: Tuberculosis.

before the pandemic. However, the difference between the 2 groups was not statistically significant (P > .05). All clinical characteristics of ALRI in the form of fever, cough, and shortness of breath showed significant differences during and before the pandemic (P < .05), but temperature and respiratory rate parameters did not show statistically significant differences (P > .05). Significant differences were also observed in terms of comorbidities including CHD, tuberculosis, immunosuppression, malignancy, and asthma (P < .05). There was no significant difference in patient outcomes between before and during the pandemic (P > .05). The average length of hospital stay for patients was found to be longer during the pandemic, which was 13 days, when compared to before the pandemic (P < .05).

The comparison of supporting examinations results of ALRI cases before and during the pandemic is shown in Table 3. Significant differences were observed in terms of Neutrophil-to-lymphocyte ratio (NLR) and total lymphocytes (P < .05), while the results of other tests showed no statistically significant differences (P > .05). The mean leukocyte count, NLR, total lymphocyte, C-Reactive Protein (CRP), and procalcitonin were found to be higher during the COVID-19 pandemic. A significant difference was also seen in the findings of complications on chest X-ray (P < .05).

During the COVID-19 pandemic, rapid antigen examination was carried out in 115 cases (28.1%) and SARS-CoV2 PCR examination was done in 229 cases (56%). A total of 13 cases (11.3%) showed reactive results on rapid antigen examination and 16 cases (4.9%) were positive on nasopharyngeal and oropharyngeal swab examination using the RT-PCR method.

[‡]Mean (range).

Variable	Before the pandemic	During the pandemic	P value
Peripheral blood test [‡]			
Hb (g/dL)	10.7 (2.5-23.2)	10.6 (1.3-36.7)	.367*
Ht (%)	32.3 (3.0-63.4)	31.8 (4.8-73.8)	.497*
Leukocyte (uL)	16547 (290-627000)	21271 (490-528000)	.302*
Platelet (uL)	331 469 (1030-1 287 940)	320512 (1000-1022000)	.201*
NLR	3.1 (0.03-98)	4.1 (0.1-46.8)	.007*
Total lymphocyte	4890 (65-49 973)	4972 (49-120790)	.003*
CRP level [†]			.660**
Increased	404 (78.3)	224 (77.0)	
Normal	112 (21.7)	67 (23)	
Mean (range)	4.4 (0.01-57.2)	4.7 (0.01-37.4)	.773*
Procalcitonin level [†]			.669**
Increased	17 (12.9)	11 (15.7)	
Normal	115 (87.1)	59 (84.3)	
Mean (range)	5,8 (0.01-161.4)	21.7 (0.02-370)	.082*
Blood culture examination [†]			.630**
Microorganisms found	65 (12.2)	16 (3.9)	
Sterile	321 (60.1)	66 (16.1)	
Not inspected	148 (27.7)	327 (80)	
Chest X-ray [†]			.018**
With complications	50 (9.4)	21 (5.1)	
No complications	484 (90.6)	388 (94.9)	

Table 3. Differences in the Supporting Examination Characteristics of ALRI Cases.

CRP normal range <0.3 mg/dL, procalsitonin normal range <0.5 ng/mL.

*Chi-square test.

**Mann-Whitney test.

†n (%).

[‡]Mean (range).

Table 4. Outcomes.

	Outcomes			
Groups	Died	Survived	P value*	RR (CI 95%)
Before the pandemic (n = 534)	116 (21.7%)	418 (78.3%)	.777	1.03 (0.81-1.32)
During the pandemic $(n = 409)$	92 (22.5%)	317 (77.5%)		

*Chi-square test.

Comparison of patient outcomes in the 2 study groups is depicted in Table 4. During the COVID-19 pandemic, there were 22.5% deaths in ALRI patients, while the pre-pandemic mortality rate was 21.7%. However, the outcomes between these 2 groups did not show a statistically significant difference (P > .05).

Discussion

Acute lower respiratory infections (ALRI) include respiratory tract infections under the laryngeal structure consisting of epiglotitis, laryngotracheobronchitis (croup), bronchitis, bronchiolitis, and pneumonia. While there is a classification based on anatomical function consisting of 2 functional compartments, namely the conduction zone and the respiratory zone. In this study, acute lower respiratory infections consisted of infections from the respiratory zone. The COVID-19 pandemic has affected various aspects of life around the world, and one of the impacts of this pandemic is its impact on aspects of health care. The results of this study indicate that the prevalence of ALRI in pediatric patients has decreased during the COVID-19 pandemic when compared to before the COVID-19 pandemic, these findings were obtained from national referral hospitals that have not been spared the impact of the COVID-19 pandemic. The Large-Scale Social Restrictions policy implemented by the government as an effort to prevent the transmission of COVID-19 can also limit people's mobility, including in efforts to visit health service centers including Dr. Hasan Sadikin General Hospital Bandung.^{6,7}

The decrease in the number of hospital visits during the COVID-19 pandemic has been widely reported in previous publications. The CDC in their weekly morbidity and mortality report for June 2020, reported that during the initial 4-week interval of the COVID-19 pandemic, emergency department visits were lower than during the same 4-week period in the previous year, with cases dominated by life-threatening patients that cannot be treated in primary health facilities.⁸ A study conducted at an Israeli teaching hospital previously reported similar findings, where there was a decrease in the number of pediatric emergency department visits during the 2020 pandemic when compared to the number of visits in 2019.⁹

Dr. Hasan Sadikin General Hospital Bandung as the highest referral center implements a tiered referral system, with every hospital in West Java able to use the integrated referral system (SISRUTE) so that through this system patients can get appropriate medical treatment. This referral system was implemented before the COVID-19 pandemic. Patients who already have national health insurance (BPJS) will be integrated with SISRUTE and receive services at primary, secondary, or tertiary health facilities, according to their needs. The results of this study showed that the number of referral patients was higher during the COVID-19 pandemic (47.4%) when compared to before the pandemic (19.9%). This could be related to the increased need for diagnosis and the limited availability of distinct isolation rooms during the COVID-19 pandemic in peripheral hospitals, so patients with ALRI need to be referred to Dr. Hasan Sadikin General Hospital Bandung as the highest referral center in West Java with the availability of diagnostic aid and isolation rooms specifically provided during the COVID-19 pandemic.

Male ALRI patients were preponderance on both of period 1 year of pandemic (59.4%) and before the pandemic (58.6%). This finding is in line with previous studies conducted on hospitalized ALRI patients in Iran,⁵ East Nusa Tenggara,¹⁰ Lebanon,¹¹ and China.¹²

During the pandemic, most patients with ALRI were aged <1 year (42.8%), whereas before the pandemic most of the patients were aged 1 to <5 years (51.9%). Other study reports in various other countries have also shown that the hospitalization rate for patients with ALRI is highest in children younger than 1 year of age and the prevalence decreases with age. Some of the causes that can influence this are decreased risk exposure, improved nutrition, and possibly improved

management of ALRI in primary and secondary health facilities. The age range of 1 to <5 years is a period of introducing complementary foods and breastfeeding weaning. This is associated with increased exposure risk in this age group and passive antibody weaning from the mother which may have an impact on the incidence of ALRI in the under-5 age group. The most common risk factors for exposure in this age group include malnutrition, dense and slum dwellings, exposure to indoor air pollution, and low birth weight.^{1,5,11,13,14}

All clinical characteristics of ALRI, including fever, cough, and shortness of breath, showed significant differences between during and before the COVID-19 pandemic. In a study conducted by Chen et al¹² involving 1992 subjects during the pre-pandemic period, clinical symptoms of cough were found in 68% of cases, followed by fever in 51.9% of cases. Fever and cough are clinical markers of ALRI in all age groups. Other respiratory symptoms that can be found include tachypnea, increased respiratory effort characterized by chest wall indrawing to nasal flaring, as well as hypoxia. During the COVID-19 pandemic, confirmed cases of ALRI in East Nusa Tenggara showed similar symptoms, namely cough (81%) and fever (69%).¹⁰ Fever and respiratory symptoms are the basis for the diagnosis of ALRI which were then further supported by evidence of pulmonary parenchymal involvement on physical examination or the findings of infiltrates on chest radiography.^{10,12,15}

In terms of comorbid conditions that are CHD, TBC, immunosuppression, malignancies, and asthma, showed significant differences in both period. Immunosuppressed conditions (62.7%), CHD (58.4%), and then TBC (56.6%) were the 3 most common comorbidities found in patients with ALRI before the COVID-19 pandemic. The results of this study are different from the results of a study in Iran in 2018, where in patients with ALRI, the most common underlying diseases were asthma, bronchial hyperactivity, and cystic fibrosis which manifested in the lungs, and neurological diseases such as spinal muscular atrophy (SMA), polymyalgia rheumatica (PMR), and cerebral palsy (CP).⁵ During the COVID-19 pandemic, patients with comorbid CHD and TBC were still at the top of the list, and malignancies, immunosuppression, and asthma, respectively, became other comorbidities that accompany patients with ALRI. Of all ALRI patients during the COVID-19 pandemic, only 16% of patients had comorbidities, in line with a previous study by Indrivani et al¹⁰ which found that 29% of patients had comorbidities while being treated. Comorbidities that accompany that study population include asthma, malignancy, CHD, and epilepsy.

At the beginning of COVID-19 pandemic, rapid antigen SARS-CoV2 examination was performed to patient with ALRI instead of PCR because of limited availability of tools and reagents as well as the results of the examination it took a long time unlike now. A total of 13 of 115 cases (11.3%) showed reactive results on rapid antigen examination and 16 of 229 cases (4.9%) were positive on nasopharyngeal and oropharyngeal swab examination.

There were no significant differences in patient outcomes before and during the pandemic. The average length of hospital stay was found to be longer during the COVID-19 pandemic, which was 13 days, and showed a significant difference when compared to the length of treatment before the pandemic. This could be due to the time required for the RT-PCR swab examination as the gold standard in determining the exposure status of being infected with COVID-19. The results of the examination at the beginning of the 2020 pandemic period are known to take a maximum of 5 to 7 days. In line with the increase in the number of cases of COVID-19 as well as the development of rapid molecular testing, the examination of the COVID-19 exposure status has become possible in only 4 to 24 hours using conventional methods after samples are sent, except on Sundays which are the time for the device maintenance. In addition to the supporting examinations that take time, the availability of ward rooms is also another obstacle associated with the length of stay in the hospital. Patients who do not receive isolation treatment rooms or patients with severe conditions who require intensive isolation rooms will be temporarily placed in a specific isolation room in the emergency department with limited availability of other tools and support devices.

Conclusion

The prevalence of ALRI in children during the COVID-19 pandemic is lower compared to before COVID-19 pandemic and there are differences its the characteristics of ALRI in children before and during the COVID-19 pandemic at Dr. Hasan Sadikin General Hospital Bandung such as referral status, age, nutritional status, clinical characteristics in the form of fever, cough, shortness of breath, and a comorbidities.

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Author Contributions

HMN conceptualized and designed the study and was involved in first drafting the manuscript, and critical revision. AM, PI were involved in drafting the manuscript, analysis or interpretation of data, and critical revision. All authors finalized the manuscript and all agreed of the manuscript.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical Approval

This study was conducted after an approval is obtained from the Research Ethics Committee of the Faculty of Medicine, Universitas Padjadjaran with a registration number of LB.02.01/X.6.5/150/2021.

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