Published online: 2020-01-02

Pulmonary Hypertension in Children with Lower Respiratory Tract Infections in the Konya Province of Turkey

Yeter Düzenli Kar[1,2] Fatih Akın[3] Ahmet Sert[4] Şükrü Arslan[5]

[1] Division of Pediatric Hematology/Oncology, Department of Pediatrics, Erzurum Regional Training and Research Hospital, Erzurum, Turkey
[2] Department of Pediatrics, Konya Training and Research Hospital, Konya, Turkey
[3] Department of Pediatrics, Meram Medical Faculty, Necmettin Erbakan University, Konya, Turkey.
[4] Division of Pediatric Cardiology, Department of Pediatrics, Selçuk University Medical School, Konya, Turkey
[5] Division of Pediatric Rheumatology, Department of Pediatrics, Selçuk University Medical School, Konya, Turkey

Address for correspondence Yeter Düzenli Kar, MD, Division of Pediatric Hematology/Oncology, Department of Pediatrics, Erzurum Regional Training and Research Hospital, 25080 Erzurum, Turkey (e-mail: yeterduzenli@yahoo.com).

J Pediatr Infect Dis 2020;15:95–101.

Abstract

Objective Lower respiratory tract infections (LRTI) are one of the most important causes of morbidity and mortality in childhood. Hypoxemia, pulmonary hypertension (PH) due to pulmonary vasoconstriction, and heart failure due to various causes are the most important risk factors for mortality in LRTI. The aim of this study was to investigate characteristics of the patients with LRTI and the frequency of PH that developed secondary to LRTI.

Materials and Methods The study included 70 patients who were diagnosed as having LRTI clinically and radiologically between January 2012 and March 2013 at Department of Pediatrics, Konya Training and Research Hospital. Age, sex, risk factors for LRTI, symptoms and physical examination findings, laboratory tests, and Doppler echocardiography findings of the patients were retrospectively reviewed.

Results Of the patients, 44 (62.9%) were male and 26 (37.1%) were female. Thirty-seven (52.9%) patients were younger than 1 year, and the mean age was 2.5 ± 3.11 years. The most common symptoms of the patients were cough and fever. Rhonchus, retraction, and crackles were found to be the most common findings in physical examinations. Heart failure was found in 10% of patients and PH was detected in 8.6% through Doppler echocardiography. Development of heart failure and the presence of bilateral patch infiltration on posteroanterior chest X-rays were significantly more frequent in patients with PH. Some 42.9% of patients had at least one viral agent in their nasopharyngeal swabs. The most common viral agents were respiratory syncytial virus and rhinoviruses.

Conclusion PH may develop during the course of LRTI in children. Given that the development of PH can cause life-threatening complications such as heart failure, affected patients should be kept under close follow-up. It should be remembered that PH is more likely to develop in patients with bilateral patch infiltration on chest X-ray.

Keywords
- children
- lower respiratory tract infections
- pulmonary hypertension

received
June 21, 2019
accepted after revision
November 14, 2019
published online
January 2, 2020

Copyright © 2020 by Georg Thieme Verlag KG, Stuttgart · New York

DOI https://doi.org/10.1055/s-0039-3401984.
ISSN 1305-7707.

Downloaded by: Karolinska Institutet. Copyrighted material.

Introduction

Lower respiratory tract infections (LRTI) are among the most important causes of morbidity and mortality in childhood. More than 700,000 children under the age of 5 years die of LRTI every year.[1] The pathophysiology of LRTI includes bronchitis, acute bronchiolitis, and pneumonia. Bronchiolitis affects the smallest branches of the bronchial tree in children at <2 years of age and most often has viral etiology.[2] Pneumonia is an acute inflammation that develops in the lung parenchyma (alveoli and interstitium) in response to infectious or noninfectious agents such as bacteria and viruses. It occurs when pathogenic viruses and bacteria invade the mucosa in the upper respiratory tract and spread to the lower respiratory tract.[3] Viruses are usually responsible for LRTI and respiratory syncytial virus (RSV), rhinoviruses, influenza A and B, parainfluenza virus, and adenoviruses have been identified as the main causative factors.[4]

Hypoxemia is the most significant risk factor for all LRTI-related deaths, and hospitalization is shortened[5] and requirement of mechanical ventilator and mortality rates are significantly reduced by detecting hypoxemia via pulse oximetry and providing oxygen therapy.[6] Furthermore, heart failure developed due to various causes contributes to mortality in LRTI.[7] Heart failure may develop due to direct damage to the myocardium by circulating toxins and microorganisms, disruption of the balance between right ventricular afterload and preload due to hypoxemia, and increased pulmonary artery pressure (PAP) due to pulmonary vasoconstriction (pulmonary hypertension [PH]).[8] The aim of this study was to examine the risk factors causing LRTI in children, the symptoms and physical examination findings of children with LRTI, and to investigate the frequency of PH secondary to LRTI.

Materials and Methods

The study included 128 patients who were clinically and radiologically diagnosed as having LRTI between January 2012 and March 2013 and hospitalized in the pediatric clinic in Konya Training and Research Hospital. All pediatric patients diagnosed with LRTI during the study were included in the study. Twenty-two patients with congenital heart disease accompanied by LRTI, 8 patients with bronchopulmonary dysplasia, 12 patients with asthma, 1 patient with systemic hypertension, 3 patients with chronic renal failure, 1 patient with liver failure, 10 patients with a history of prematurity (all in infancy), and 1 patient with polycythemia were excluded from the study. Echocardiographic characteristics of 70 patients who were hospitalized because of diagnosis of LRTI were recorded. Echocardiographic evaluation was performed because tachycardia, hypoxia/respiratory failure, hepatomegaly, murmur, cyanosis, pleural effusion on chest radiograph, spontaneous pneumothorax, and cardiomegaly were detected in patients. The patients' charts were reviewed retrospectively.

Children with respiratory symptoms (cough, fever, wheezing, and respiratory difficulty) and with abnormalities on physical examinations (including respiratory distress, wheezing, crackles, retraction, nasal flaring, tachypnea, and tachycardia) or with chest X-ray abnormalities (pneumonic infiltrates, pleural effusions, and atelectasis) were considered to have LRTI.

Age, sex, place of residence (urban or rural area), nursery/school attendance, presence of passive smoking, the presence of an individual who have had respiratory tract infection in the family within the last month, all symptoms (cough, fever, wheezing, loss of appetite/poor appetite, respiratory distress, restlessness, cyanosis, nausea and vomiting, and abdominal pain) and physical examination findings (body temperature, oxygen saturation [SpO_2], cyanosis, tachycardia, tachypnea, retraction, nasal flaring, crackle, rhonchus, decreased breathing sounds, hepatomegaly, and heart failure) of patients were recorded.

Patient's data were retrospectively reviewed; white blood cell count, hemoglobin, platelet count, C-reactive protein, erythrocyte sedimentation rate, procalcitonin, venous blood gas results (pH, PCO_2, and HCO_3), blood culture, nasopharyngeal swab sample (reverse transcription polymerase chain reaction [RT-PCR]) results, and Doppler echocardiography findings at the time of diagnosis were retrieved from the patient charts.

Nasopharyngeal smears were taken with swabs and transported to molecular diagnosis unit within specific liquid transport system UTM-RT transport medium (Copan, Italy). A nasopharyngeal sample was kept under −70°C until virologic tests were done. Presence and genotyping of viruses causing viral community-acquired pneumonia (CAP) were investigated with RT-PCR followed by reverse hybridization method using sequence-specific oligonucleotide probes (SSOP) with three steps. First, RNA isolation were performed with isolation kits RTP DNA/RNA Virus Mini Kit (Invitek, Germany) and then, in vitro amplification was performed via specific biotin labeled primers by using thermal cycler (Bioer XP Cycler, Japan), and finally, the amplification products were selectively hybridized to the nitrocellulose test strips (GenID GmbH, CAPvir Straßberg, Germany) which contain SSOP with AutoLiPA instrument (Tecan ProfiBlot T48, Austria). Each strip contained five specific probes for genotyping of the most common causative agent of the viral CAP.

Chest X-rays were evaluated together with a radiologist.

Ethical Issues

This study was approved by the local ethics committee of Necmettin Erbakan University, Konya, Turkey.

Transthoracic Echocardiography

All individuals included in the study underwent two-dimensional, colored M-mode and pulsed wave Doppler echocardiography, which was performed by the pediatric cardiologist at the pediatric cardiology unit of our hospital within the first 24 hours after admission. A ProSound Alpha 7 Aloka (Hitachi-Aloka Medical, Tokyo, Japan) echocardiography device was used. The transducer had a frequency of 3 to 7 MHz.

Individuals were placed in the supine or left lateral position to obtain an optimal image with two-dimensional echocardiography. Both atria and ventricles, interventricular and interatrial septum, mitral, tricuspid, aortic and pulmonary valves, pulmonary artery, aorta, and cardiac cavities

Downloaded by: Karolinska Institutet. Copyrighted material.

were evaluated in the long axis, apical four-chamber cavities, short parasternal, subcostal, and suprasternal positions. All echocardiographic measurements and Doppler evaluations were performed by a specialist pediatric cardiologist who was blind to the clinical and laboratory findings of the study. Transthoracic echocardiography was further used to calculate the estimated pulmonary artery systolic pressure.

Continuous wave Doppler of the peak tricuspid regurgitation (TR) velocity was taken as a basis for the calculation of PAP. The simplified Bernoulli's equation ($\delta p = 4V^2 = 4 \times [\text{TR velocity}]^2$) was based on the relationship between TR velocity and peak pressure gradient in TR.

Pulmonary artery systolic pressure was calculated using the following formula: TR pressure gradient + right atrial pressure (10 mm Hg). Patients with PH in the first echocardiographic examination were subject to a second echocardiography examination after treatment. Patients with PAP more than 35 mm Hg on echocardiographic examination were considered as having PH.

The diagnosis of heart failure was made with physical examination findings and echocardiographic findings. According to the echocardiography, the group with ejection fraction less than 40% was classified as heart failure with low ejection fraction, the group with 50% and more was classified as heart failure with preserved ejection fraction group, and the group with ejection fraction between 40 and 49% was classified as heart failure with midrange ejection fraction group.

Statistical Analysis

Statistical analysis was performed using the SPSS version 15.0 software. A p-value of <0.05 was considered statistically significant.

Results

The demographic characteristics and family history of the patients are shown in ►**Table 1**. Of the patients, 44 (62.9%) were male and 26 (37.2%) were female. The mean age was 2.5 ± 3.11 years (min: 1.5 months, max: 14.5 years). Of the patients, 37 (52.9%) were aged under 1 year, 20 (28.6) were aged between 1 and 4 years, 10 (14.3%) were aged between 5 and 9 years, and three (4.3%) were aged between 10 and 15 years. PH was detected noninvasively in 8.6% of the patients using Doppler echocardiography (►**Table 1**). Doppler echocardiography examinations were repeated following the regression of LRTI findings in patients with PH, and the PAP of the patients was observed to be improved after LRTI.

►**Table 2** presents the laboratory results of nasopharyngeal swab samples from 70 patients and blood culture samples obtained from 33 of 70 patients. At least one viral agent was detected in nasopharyngeal swab samples of 30 patients. A bacterial agent was detected in only one of the blood culture samples obtained from 33 patients. Of the 30 patients with a viral agent, 1 had adenovirus (1.4%), 1 had coronavirus 229-E/N163 (1.4%), 1 had metapneumovirus (1.4%), 2 had parainfluenza virus type 3 (2.8%), 2 had RSV-A (2.8%), 5 had RSV-B (7.1%), 1 had bocaviruses 1, 2, 3, and 4 (1.4%), 5 had rhinoviruses A, B, and C (7.1%), 2 had adenovirus + rhinoviruses A, B, and C (2.8%), 1 had coronavirus Oc43 + rhinoviruses A, B, and C (1.4%), 1 had parainfluenza virus type 3 + bocaviruses 1, 2, 3, and 4 (1.4%), 2 had rhinoviruses A, B, and C + RSV-B (2.8%), 2 had rhinoviruses A, B, and C + bocaviruses 1, 2, 3, and 4 (2.8%), 1 had RSV-A + metapneumovirus (1.4%), 2 had RSV-B + bocaviruses 1, 2, 3, and 4 (2.8%), and 1 had rhinoviruses A, B, and C + RSV-A + parainfluenza virus type 4 (1.4%). *Staphylococcus warneri* was detected in the blood culture sample of one patient (3.03%) and no growth was detected in the other patients.

Of six patients with PH(+), rhinoviruses A, B, and C + RSV-B were detected in one, RSV-A in one, and bocaviruses 1, 2, 3, and 4 were detected in one patient. No difference was observed between the PH and non-PH groups in terms of isolated microorganisms.

The symptoms and findings on physical examination of the study patients are shown in ►**Table 3**. The most common symptoms were cough, fever, and wheezing. At the time of admission, 34 (48.57%) patients had fever more than 38°C, which was determined through axillary measurements. Twenty-one patients (30%) had an SpO_2 of ≤ 92. The most common physical findings of the patients were rhonchi,

Table 1 Demographic, familial characteristics of patients, and transthoracic echocardiography results

Demographic characteristics		
Age (y) mean (±SD)	2.5 ± 3.11	
Median (lower–upper limit)	1	1.5 mo–14.5 y
Sex	*N*	%
Male	44	62.9
Female	26	37.2
Place of residence		
Urban area	58	82.9%
Rural area	12	17.1%
Familial characteristics–risk factors	*N*	%
A family history of asthma–atopy	14	20
Passive smoking	46	65.7
The presence of an individual who have had respiratory tract infection in the family within the last month	15	21.4
The presence of individuals who go to school or daycare	33	47.1
Echocardiography	**Mean ± SD**	**Median (lower–upper limit)**
TR velocity (m/s)	2.1 ± 0.4	2.1 (1.3–3.7)
TR gradient (mm Hg)	19.09 ± 7.7	17.5 (7–57)
Calculated PAP from TR (mm Hg)	29.09 ± 7.7	27.5 (17–67)
Pulmonary hypertension *n* (%)	6	8.6%

Abbreviations: PAP, pulmonary artery pressure; SD, standard deviation; TR, tricuspid regurgitation.

Downloaded by: Karolinska Institutet. Copyrighted material.

Table 2 Microbiological findings of patients

Nasopharyngeal swab samples	%
Adenovirus	1.4
Coronovirus 229 E/Nl63	1.4
Metapneumovirus	1.4
Parainfluenza virus type 3	2.8
RSV-A	2.8
RSV-B	7.1
Bocaviruses 1, 2, 3, 4	1.4
Rhinoviruses A, B, C	7.1
Adenovirus + rhinoviruses A, B, C	2.8
Coronovirus Oc43 + rhinoviruses A, B, C	1.4
Parainfluenza virus type 3 + bocaviruses 1, 2, 3, 4	1.4
Rhinoviruses A, B, C + RSV-B	2.8
Rhinoviruses A, B, C + bocaviruses 1, 2, 3, 4	2.8
RSV-A + metapneumovirus	1.4
RSV-B + bocaviruses 1, 2, 3, 4	2.8
Rhinoviruses A, B, C + RSV-A + parainfluenza virus type 4	1.4
Blood culture	
Staphylococcus warneri	3.03

Abbreviation: RSV, respiratory syncytial virus.

retraction, crackles, and tachypnea, respectively. There was no significant difference between the patients with LRTI with and without PH in terms of symptoms; however, heart failure was found significantly more frequently in the group with PH (►**Table 3**).

According to the echocardiography, one of our patients with an ejection fraction less than 40% was diagnosed as having severe heart failure, five patients (ejection fraction between 40 and 49%) were diagnosed as having midrange heart failure, and one patient (ejection fraction more than 50%) was diagnosed as having heart failure with preserved ejection fraction. Clinically, hypotension and shock status were not detected in any of our patients.

Posteroanterior (PA) chest X-rays of the patients taken at the time of admission revealed that all patients had LRTI findings radiologically (►**Table 4**). In addition to infiltration findings on the chest X-rays of the patients, there was pleural effusion in four patients, atelectasis in three patients, and pneumothorax in one patient.

When the patients with and without PH were compared in terms of PA chest X-ray findings and laboratory parameters, PH was found to be significantly more common in patients with bilateral patch infiltration on PA chest X-ray (►**Table 4**).

Twenty-three of our patients required oxygen, and three required invasive mechanical ventilation. Five patients underwent noninvasive mechanical ventilation (continuous positive airway pressure), and 15 received oxygen support through a nasal mask or nasal cannula. Eight patients were managed in the intensive care unit. Three patients with PH

Table 3 Comparison of symptoms and physical examination findings of the patients with and without pulmonary hypertension

	With PH ($n = 6$)	Without PH ($n = 64$)	*p*-Value
Symptoms			
Fever	6 (100%)	55 (85.9%)	0.329
Cough	6 (100%)	64 (100%)	0.999
Wheezing	6 (100%)	53 (82.8%)	0.272
Respiratory distress	4 (66.7%)	52 (81.3%)	0.397
Cyanosis	1 (16.7%)	20 (31.3%)	0.459
Restlessness	5 (83.3%)	51 (79.7%)	0.832
Nausea and vomiting	1 (16.7%)	15 (23.4%)	0.708
Abdominal pain	1 (16.7%)	4 (6.3%)	0.347
Loss of appetite/ poor appetite	6 (100%)	51 (79.7%)	0.225
Physical examination findings			
Body temperature (°C) mean (±SD)	37.8 ± 0.9	37.6 ± 0.9	0.666
Median (lower–upper limit)	38 (36.2–39)	37.8 (36–39)	
SpO_2 mean (±SD)	90.8 ± 8.9	94.03 ± 7.5	0.187
Median (lower–upper limit)	93 (74–98)	96.5 (61–100)	
Tachycardia (*n*, %)	3 (50%)	30 (46.9%)	0.884
Cyanosis	1 (16.7%)	7 (10.9%)	0.689
Tachypnea	3 (50%)	35(54.6%)	0.826
Retraction	5 (83.3%)	42 (65.6%)	0.381
Nasal flaring	2 (33.3%)	29 (45.3%)	0.575
Crackles	3 (50%)	36 (56.3%)	0.77
Rhonchus	5 (83.3%)	51 (79.7%)	0.832
Decreased breathing sounds	0	5 (7.8%)	0.481
Tuber sufl	1 (16.7%)	4 (6.3%)	0.347
Hepatomegaly	2 (33.3%)	9 (14.1%)	0.218
Heart failure	2 (33.3%)	5 (7.8%)	**0.048**

Abbreviations: PH, pulmonary hypertension; Respiratory distress, tachypnea, dyspnea, chest wall withdrawal; SpO_2, oxygen saturation.

required oxygen, two received invasive mechanical ventilation therapy, and one received noninvasive mechanical ventilation (continuous positive airway pressure).

One patient in whom RSV-A was isolated developed spontaneous pneumothorax. The patient underwent mechanical ventilation due to poor lung ventilation, but later died.

Discussion

LRTI is the main cause of morbidity and mortality due to infectious disease in children aged under 5 years around the world.[2,9] It is an important public health problem that is costly in terms of medical and socioeconomic aspects due to multiple polyclinic examinations, hospitalization, and loss of

Downloaded by: Karolinska Institutet. Copyrighted material.

Table 4 Comparison of PA chest X-rays and laboratory parameters of patients with and without pulmonary hypertension

	With PH ($n = 6$)	Without PH ($n = 64$)	p-Value
Radiological findings			
Reticular infiltration	1 (16.7%)	29 (45.3%)	0.178
Reticulonodular infiltration	3 (50%)	14 (21.9%)	0.127
Unilateral lobar involvement	0	13 (20.3%)	0.225
Unilateral patch infiltration	1 (16. 7%)	3 (4.7%)	0.230
Bilateral patch infiltration	2 (33.3%)	4 (6.3%)	**0.024**
Pleural effusion	1 (16.7%)	3 (4.7%)	0.230
Atelectasis	1 (16.7%)	2 (3.1%)	0.120
Pneumothorax	0	1 (1.6%)	0.759
Laboratory parameters of patients			
White blood cell count (/mm^3) (mean ± SD)	17,470 ± 12,708	12,895 ± 6,001	0.753
Median (lower–upper limit)	12,600 (6,580–36,490)	12,205 (3,350–31,670)	
CRP (mg/L) (mean ± SD)	45.6 ± 42.6	31.2 ± 48.1	0.348
Median (lower–upper limit)	39.4 (2.97–108)	8.97 (2.97–204)	
ESR (mm/h) (mean ± SD)	48.5 ± 22.4	30.3 ± 26.4	0.065
Median (lower–upper limit)	42.5 (31–91)	22 (1–121)	
Procalcitonin (ng/mL) (mean ± SD)	0.33 ± 0.37	0.62 ± 1.33	0.315
Median (lower–upper limit)	0.18 (0.1–0.89)	0.1 (0.02–5.59)	
Blood gas			
PH (ort. ± SD)	7.35 ± 0.07	7.36 ± 0.06	0.992
Median (lower–upper limit)	7.37 (7.23–7.42)	7.37 (7.13–7.46)	
PCO_2 (mm Hg) (mean ± SD)	41.4 ± 9.8	39.5 ± 9.3	0.469
Median (Lower–upper limit)	39.6 (30–59)	37.8 (24–69)	
HCO_3 (mmol/L) (mean ± SD)	23.23 ± 3.64	21.9 ± 2.9	0.256
Median (lower–upper limit)	23.85 (17–27)	22 (15–35)	

Abbreviations: CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; PA, posteroanterior; PH, pulmonary hypertension; SD, standard deviation.
Notes: 1. Bold represents p-value < 0.05 that was considered statistically significant. 2. PH was found to be significantly more common in patients with bilateral patch infiltration on PA chest X-ray.

Downloaded by: Karolinska Institutet. Copyrighted material.

parents' working hours.[2] In line with the literature, the majority of the patients in our study were male and aged 1 year or younger.[10] Factors paving the way for LRTI such as the history of passive smoking, family history of asthma–atopy, at least one family member who had a respiratory tract infection in the last month, a sibling going to school or daycare,[11] and living in the city center[12] were detected.

At least one viral agent was detected in 30 (42.9%) of our patients. A viral agent was detected in 18 patients (25.7%) and viral coinfection was found in 12 patients (17.1%). In patients with one viral agent, RSV-B and rhinoviruses A, B, and C were the most common agents. Of the 12 patients with viral coinfection, 11 (15.7%) had two and 1 had three viral infectious agents. Shafik et al[12] reported the frequency of viral agents as 59.9%, the detection rate of two or more viral infectious agents (viral coinfection) as 10.8%, and RSV and parainfluenza virus as the most commonly isolated agents. Kurskaya et al[9] reported the frequency of viral agent as 72.3%, the rate of viral coinfection as 14.5%, and RSV, influenza, and rhinovirus as the most commonly isolated agents. Korsun et al[2] reported the frequency of viral agent as 78.1%, the rate of viral coinfection as 15.9%, and RSV and rhinovirus as the most commonly isolated agents. Akçalı et al[4] reported the frequency of viral agents as 41.8% and RSV and rhinovirus as the most commonly detected agents. The results of our study were similar to the literature. No difference was observed between the PH and non-PH groups in terms of isolated microorganisms. We think that the reason why no difference was detected in terms of isolated microorganisms is the small number of patients included in the study.

The most common symptoms at the time of admission were cough (100%), fever (87.1%), wheeze (84.3%), loss of appetite/poor appetite (81.4%), dyspnea, and restlessness (80%) in the present study. A literature review revealed considerable variation in the symptomatology of children with LRTI. The most common symptoms reported by Jiang et al[13] were cough (94.3%), wheeze (28.1%), tachypnea (5.1%), and dyspnea (2.1%). Ma et al[14] found the commonest symptoms to be fever (99.2%), cough (96.9%), and tachypnea (22.8%); in a study by Berg et al,[15] the commonest symptoms were fever (80.8%),

cough (89.4%), tachypnea (75.8%), and wheeze (18.1%); and in a study by Cevey-Macherel et al,[16] they were cough (97%), malnutrition (81%), vomiting (45%), and abdominal pain (17%).The reason for the more frequent detection of symptoms during admission to hospital compared with the literature can be attributed to the fact that all of our patients required hospitalization.

The most important physical examination finding of LRTI in children is the presence of tachypnea, as well as cough and fever. The presence of tachypnea is the main finding in distinguishing LRTI from upper respiratory tract infections. Other common physical examination findings were reported as crackles, rhonchi, wheezing, cyanosis, dyspnea, nasal flaring, chest retraction,[17] heart failure, and PH.[8] In a study[18] conducted in Turkey, the most common physical examination findings were fever (46%), tachypnea (82%), SpO_2 of $<92\%$ (27%), rales (70%), and recession (82%). In another study including 265 children with CAP, fever (80.8%), tachypnea (70%), SpO_2 of $\leq 92\%$ (11.6%), wheezing (21.7%), fine rales (20.9%), and decreased breath sounds (8.5%) were reported as the most common findings. In the present study, 34 (48.57%) patients were found to have a fever of $\geq 38°C$ through axillary measurements at the time of admission. Twenty-one patients (30%) had an SpO_2 of ≤ 92. Other common findings detected in the present study were rhonchi (80%), retraction (67.1%), crackles (55.7%), and tachypnea (54.2%). Our findings were compatible with the results of previous studies.

Both the cardiovascular and respiratory systems need to be physiologically strong for the cardiorespiratory system to maintain effective function. A change in cardiorespiratory interaction for any reason can lead to significant changes in cardiac function.[8] There are several reasons for congestive heart failure (CHF) in patients with LRTI. One of them is that the respiratory hypoxia in LRTI causes pulmonary vasoconstriction. PH causes right ventricular dysfunction and therefore contributes to the development of heart failure in these cases. Hypoxia also depresses myocardial function, disrupts the balance between afterload and preload, and as a result, may lead to heart failure.[7] Myocarditis caused by microorganisms invading the heart muscle directly is also one of the factors causing heart failure.[8,19] In the literature, multivariable results have been reported regarding the incidence of CHF in patients with LRTI. In various studies, the incidence of CHF in children with LRTI was reported as 10 to 72%.[7,19–22] In the present study, CHF was detected in 10% of patients with LRTI.

Considering the studies evaluating the prevalence of PH via Doppler echocardiography in children with LRTI, the prevalence of LRTI-associated PH was 33.3% in children with pneumonia and 15% in children with bronchiolitis in a study by Kabir et al,[7] and 24% in 75 infants with acute respiratory disease in a study by Bardi-Peti and Ciofu.[23] Üner et al[24] and Sreeram et al[25] reported prevalence of, respectively, 40.5% in children with pneumonia and 52.38% in children with acute bronchiolitis. In a study in 93 healthy infants with RSV infection, PH was found in 22%, and PH during RSV infection was a poor prognostic indicator in healthy infants without underlying illnesses.[26] In another study, 154 infants with RSV bronchiolitis were evaluated, and it was reported that the development of PH was often associated with triggering congenital heart disease and chronic lung disease; the authors suggested that echocardiographic examination during RSV bronchiolitis was unnecessary unless there was shock or poor perfusion in a previously known infant.[27] In another study,[28] right ventricular insufficiency secondary to PH was reported in 26% of patients. In the present study, PH was detected in 8.6% of patients. The incidence of CHF and PH was found to be lower in our study. We believe that the reason for this is that patients with underlying chronic diseases were excluded from the study, and patients were diagnosed and treated early because of the easier access to health services in recent years.

The following can be observed on the PA chest X-rays of patients with LRTI: reticular infiltration, reticulonodular infiltration, unilateral lobar involvement, bilateral patch infiltration, unilateral patch infiltration, pleural effusion, atelectasis, and pneumothorax.[29] Radiological findings were present in the PA chest X-rays of all our patients, the most common of which were reticular and reticulonodular infiltration. This supports the fact that viral agents are responsible for the majority of LRTI.[2,4]

The laboratory findings and symptoms did not predict the risk of developing PH because the present study compared patients with and without PH, and heart failure and PA infiltration were found to be more common in patients with PH.

The limitations of our study include having a small number of patients, being a single-center trial, and the lack of tests such as creatine kinase-MB and N-terminal pro-B-type natriuretic peptide in the diagnosis of heart failure in our hospital. Also, PH diagnoses were not confirmed using right heart catheterization.

In conclusion, it has been emphasized that PH may develop in children with LRTI (8.6%), which can cause serious and life-threatening complications such as heart failure; affected patients should therefore be kept under close follow-up. Patients with bilateral patch infiltration on chest X-ray were found to be more at risk in terms of PH development. Furthermore, compatible with the existing literature, the most common viral agents were found to be RSV and rhinoviruses. We believe that regional data reported from the world and Turkey for LRTI will also be guiding for vaccine development methods, which have been studied extensively.

Conflict of Interest
None declared.

References

1 GBD 2015 LRI Collaborators. Estimates of the global, regional, and national morbidity, mortality, and aetiologies of lower respiratory tract infections in 195 countries: a systematic analysis for the Global Burden of Disease Study 2015. Lancet Infect Dis 2017;17 (11):1133–1161
2 Korsun N, Angelova S, Trifonova I, et al. Viral pathogens associated with acute lower respiratory tract infections in children younger than 5 years of age in Bulgaria. Braz J Microbiol 2019;50(01):117–125
3 Mani CS, Murray DL. Acute pneumonia and its complications. In: Long SS, Pickering LK, Prober CG, eds. Principles and Practice of Pediatric Infectious Diseases, 3rd ed. Philadelphia: Elsevier Inc; 2008:245–257

Downloaded by: Karolinska Institutet. Copyrighted material.

4 Akçalı S, Yılmaz N, Güler N, et al. Frequency of respiratory viruses in children with lower respiratory tract infection. Turk Arch Ped 2013;48:215–220
5 Uygur P, Oktem S, Boran P, Tutar E, Tokuc G. Low- versus high-flow oxygen delivery systems in children with lower respiratory infection. Pediatr Int (Roma) 2016;58(01):49–52
6 Rojas MX, Granados Rugeles C, Charry-Anzola LP. Oxygen therapy for lower respiratory tract infections in children between 3 months and 15 years of age. Cochrane Database Syst Rev 2009;(01):1CD005975
7 Kabir S, Khatoon S, Fatmi L, et al. Cardiovascular changes in children with acute lower respiratory tract infection. Bangladesh Child Health. 2019;43(01):27–34
8 Corrales-Medina VF, Musher DM, Wells GA, Chirinos JA, Chen L, Fine MJ. Cardiac complications in patients with community-acquired pneumonia: incidence, timing, risk factors, and association with short-term mortality. Circulation 2012;125(06): 773–781
9 Kurskaya O, Ryabichenko T, Leonova N, et al. Viral etiology of acute respiratory infections in hospitalized children in Novosibirsk City, Russia (2013–2017). PLoS One 2018;13(09):e0200117
10 le Roux DM, Nicol MP, Myer L, et al. Lower respiratory tract infections in children in a well-vaccinated South African birth cohort: spectrum of disease and risk factors. Clin Infect Dis 2019; 69(09):1588–1596
11 Shi T, Balsells E, Wastnedge E, et al. Risk factors for respiratory syncytial virus associated with acute lower respiratory infection in children under five years: systematic review and meta-analysis. J Glob Health 2015;5(02):020416
12 Shafik CF, Mohareb EW, Yassin AS, et al. Viral etiologies of lower respiratory tract infections among Egyptian children under five years of age. BMC Infect Dis 2012;12:350
13 Jıang Y, Zhu Q, Wu J, et al. Viral etiology and clinical features of severe acute respiratory infection (SARI) in children under 5 years admitted to the Children's Hospital in Suzhou, China [in Chinese]. Fudan Univ J Med Sci 2013;40(04):407–412
14 Ma YJ, Wang SM, Cho YH, et al; Taiwan Pediatric Infectious Disease Alliance. Clinical and epidemiological characteristics in children with community-acquired mycoplasma pneumonia in Taiwan: a nationwide surveillance. J Microbiol Immunol Infect 2015;48(06): 632–638
15 Berg AS, Inchley CS, Fjaerli HO, Leegaard TM, Lindbaek M, Nakstad B. Clinical features and inflammatory markers in pediatric pneumonia: a prospective study. Eur J Pediatr 2017;176(05):629–638
16 Cevey-Macherel M, Galetto-Lacour A, Gervaix A, et al. Etiology of community-acquired pneumonia in hospitalized children based on WHO clinical guidelines. Eur J Pediatr 2009;168(12):1429–1436
17 Kocabaş E, Doğru Ersöz D, Karakoç F, et al. Çocuklarda Toplumda Gelişen Pnömoni Tanı ve Tedavi Uzlaşı Raporu. Türk Toraks Dergisi. 2009;10:5–26
18 Şişmanlar T, Aslan AT, Gülbahar Ö, Özkan S. The effect of vitamin D on lower respiratory tract infections in children. Turk Pediatri Ars 2016;51(02):94–99
19 Nimdet K, Techakehakij W. Congestive heart failure in children with pneumonia and respiratory failure. Pediatr Int (Roma) 2017; 59(03):258–264
20 İlten F, Şenocak F, Zorlu P, Teziç T. Cardiovascular changes in children with pneumonia. Turk J Pediatr 2003;45(04):306–310
21 Sadoh WE, Osarogiagbon WO. Pneumonıa complıcated by congestıve heart faılure ın Nıgerıan chıldren. East Afr Med J 2012;89(10): 322–326
22 Reshadat S. Prevalence of pneumonia among children with congestive heart failure (CHF) admitted at Shaheed Beheshti Hospital (Kermansllab-1997). J Kerman Univ Med Sci (Behbood) 2002;5:48–53
23 Bardi-Peti L, Ciofu EP. Pulmonary hypertension during acute respiratory diseases in infants. Maedica (Buchar) 2010;5(01):13–19
24 Uner A, Caksen H, Arslan S, Abuhandan M, Oner AF, Odabaş D. Doppler echocardiographic evaluation of pulmonary artery pressure in children with acute pneumonia. Acta Paediatr Taiwan 2002;43(01):10–14
25 Sreeram N, Watson JG, Hunter S. Cardiovascular effects of acute bronchiolitis. Acta Paediatr Scand 1991;80(01):133–136
26 Rodriguez-Gonzalez M, Benavente-Fernandez I, Castellano-Martinez A, Lechuga-Sancho AM, Lubian-Lopez SP. NT-proBNP plasma levels as biomarkers for pulmonary hypertension in healthy infants with respiratory syncytial virus infection. Biomarkers Med 2019;13(08):605–618
27 Kimura D, McNamara IF, Wang J, Fowke JH, West AN, Philip R. Pulmonary hypertension during respiratory syncytial virus bronchiolitis: a risk factor for severity of illness. Cardiol Young 2019; 29(05):615–619
28 Shann F, MacGregor D, Richens J, Coakley J. Cardiac failure in children with pneumonia in Papua New Guinea. Pediatr Infect Dis J 1998;17(12):1141–1143
29 Koo HJ, Lim S, Choe J, Choi SH, Sung H, Do KH. Radiographic and CT features of viral pneumonia. Radiographics 2018;38(03):719–739

Downloaded by: Karolinska Institutet. Copyrighted material.