



# Evaluation of Children with Congenital Heart Disease Hospitalized with the Diagnosis of Lower Respiratory Tract Infection

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## ABSTRACT

**Aim:** Lower respiratory tract infections are an important reason for mortality and morbidity in children with congenital heart disease. This study aimed to evaluate 50 children who had congenital heart disease and were hospitalized with lower respiratory tract infection in the Ege University Faculty of Medicine Pediatrics Hospital.

**Materials and Methods:** Fifty pediatric patients were taken into the study. Their clinical symptoms, acute phase reactants, chest X-rays, bacterial culture of transtracheal aspirate, respiratory virus panel (with multiplex polymerase chain reaction) from nasopharyngeal swab were examined. The groups were evaluated in terms of age, gender, environmental smoke exposure, living with school-aged siblings, Respiratory Syncytial virus (RSV) prophylaxis, hospitalization time, causative pathogen, additional risk factors.

**Results:** Of the 50 cases, 12 (24%) were cyanotic, 38 (76%) were acyanotic. There were 26 boys and 24 girls. The most common diagnosis in the acyanotic group was hemodynamically significant VSD (isolated or with other diagnoses) with 20 cases. The average age of the cyanotic group was 23.88±28.81, and the acyanotic group was 12.25±15.45 months old. Hospitalizations most frequently occurred in winter. The most frequent viral agent was RSV, which was not seen in the cyanotic group. All of the RSV infected patients were under 12 months old. In 16.7% of cyanotic and 52.6% of acyanotic patients there were extra risk factors such as immune deficiency, Down syndrome, prematurity, Di George syndrome, cerebral palsy, postoperative early period. Three cases lost their lives due to severe respiratory failure. There was no statistically significant difference between the two groups when compared for demographic variables, risk factors, causative pathogens, hospitalization times.

**Conclusion:** Lower respiratory tract infections and especially RSV pneumonia are important causes of mortality and morbidity in patients diagnosed with congenital heart disease. To prevent risk factors, more studies must be done.

**Keywords:** Respiratory, infections, congenital, heart, disease

## Introduction

The incidence of congenital heart disease (CHD) in the general population is about 1% and varies from 4/1000 to 50/1000 live births (1). Children with CHD have many complications concerning all of the organ systems, the respiratory system being the most important. Lower respiratory tract infection (LRTI) is a serious mortality and morbidity reason for children with CHD. Hemodynamically significant-CHD (HS-CHD) with pulmonary congestion poses

a higher risk for LRTI and hospitalizations. Respiratory Syncytial virus (RSV) pneumonia is commonly seen in the first two years of life (2). Socio-economic and environmental risk factors such as prematurity, male sex, living with school-aged siblings, exposure to environmental smoking may increase susceptibility to RSV disease and frequent hospitalizations (3,4). In this study, 50 children with CHD, who were hospitalized with the diagnosis of LRTI, were analyzed in the Ege University Faculty of Medicine Pediatrics Hospital.

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## Materials and Methods

Fifty pediatric CHD patients, aged from 1 to 108 months, hospitalized with LRTI between December 2013 and 2015 were included in our study. Ege University Faculty of Medicine Ethics Committee approved the study (approval number: 14-11/11). After being informed of the purpose and content of the study by the doctor and having read the information for patients, all the parents gave written informed consent. Exclusion criteria was refusal of parental consent to participate in the study. The eligible patients were evaluated prospectively. For these patients who were previously diagnosed or had recently been diagnosed with CHD, acute phase reactants, postero-anterior chest X-rays, bacterial culture of transtracheal aspirate, respiratory virus panel (with multiplex polymerase chain reaction) from nasopharyngeal swab were examined. Demographic and clinical data were collected from the parents. The patients were classified into two groups as cyanotic and acyanotic. The groups were examined in terms of age, gender, demographic features, additional risk factors, exposure to smoke, living with school-aged siblings, having received palivizumab prophylaxis dose, hospitalization time, causative pathogen and complications.

### Statistical Analysis

All continuous variables were analyzed using standard descriptive statistics with mean  $\pm$  standard deviation values. As qualitative variables, median, minimum and maximum values were expressed. For non-normal distribution of independent measures, Mann Whitney U test was applied to the number of categories falling into two and Kruskal Wallis H test was applied to the number of categories falling into three or more. The data sets in categorical structures were analysed with chi-square (Yates&Fisher). Statistical significance was defined as  $p < 0.05$ . All data analysis is was done with SPSS v21.0 (IBM Corporation, Armonk, New York, USA) software.

## Results

Of the 50 cases, 12 (24%) were diagnosed with cyanotic and 38 (76%) with acyanotic CHD. Boy/girl ratio was 26/24. In the acyanotic group, 6 cases (12% of 50 patients) were diagnosed with ventricular septal defect (VSD) and atrial septal defect (ASD); 6 cases (12%) with only VSD, 4 cases (8%) with only ASD; 4 cases (8%) with patent ductus arteriosus (PDA), 4 cases (8%) with endocardial cushion defect, 1 case (2%) with PDA+ASD, 1 case (2%) with aortic coarctation (AC), 2 cases (4%) with double outlet right ventricle (DORV) repair, 1 case (2%) with repair of tricuspid atresia (TA) with Fontan procedure, and 1 case (2%) with repair of d-transposition of great arteries with Jatene procedure. All the other cases had mixed type of diagnostics including VSD. In the cyanotic group, 4 cases (8%) were diagnosed with Tetralogy of Fallot (TOF), 4 cases (8%) with DORV, 2 cases (4%) with truncus arteriosus, 1

case (2%) with pulmonary atresia, 1 case (2%) with TA. The average age of the patients diagnosed with cyanotic CHD was  $23.88 \pm 28.81$  months, and that of the acyanotic CHD patients was  $12.25 \pm 15.45$  months. Six (50%) of the cyanotic and 28 (73.7%) of the acyanotic patients were infants. Seven (58.3%) of the cyanotic and 27 (71.1%) of the acyanotic patients were living with 2 or more school-aged siblings. Five (41.7%) of the cyanotic and 12 (31.6%) of the acyanotic patients had been exposed to environmental smoke (Table I). There was no statistically significant difference between the groups when compared for demographic variables, passive smoking, LRTI with viral or bacterial agent, and hospitalization time. Twenty-six of 38 acyanotic patients (68.4%) had HS-CHD before 2 years of age, and 18 of 26 (69.2%) patients received palivizumab prophylaxis dose because the other 8 patients' hospitalization was a long time away from the RSV season. In the acyanotic group, the average dose of palivizumab received was  $2.30 \pm 2.04$ . Of the 12 cyanotic patients (66.6%), 8 received palivizumab prophylaxis at an average dose of  $2.44 \pm 1.68$ . Four of them could not receive the prophylaxis because of same reason as the 8 patients in the acyanotic group. Two of the cyanotic (16.7%) and 20 of the acyanotic patients (52.6%) had extra risk factors such as immune deficiency, Down syndrome, prematurity, Di George syndrome, cerebral palsy, postoperative early

	Cyanotic n=12 (%)	Acyanotic n=38 (%)	p value
<b>Sex</b>			
Female	6 (50)	17 (44.7)	0.958
Male	6 (50)	21 (55.3)	
<b>Age</b>			
<12 months	6 (50)	28 (73.7)	0.163
$\geq$ 12 months	6 (50)	10 (26.3)	
<b>School-aged siblings</b>			
1	5(41.7)	11 (28.9)	0.438
2 or more	7(58.3)	27 (71.1)	
<b>Exposure to smoke</b>			
Yes	5 (41.7)	12 (31.6)	0.728
No	7 (58.3)	26 (68.4)	
<b>Causative viral agent</b>			
Yes	2 (16.7)	7 (18.4)	1.000
No	10 (83.3)	31 (81.6)	
<b>Causative bacterial agent</b>			
Yes	1 (8.3)	4 (10.5)	1.000
No	11 (91.7)	34 (89.5)	
<b>PICU admission</b>			
Yes	1 (8.3)	13 (34.2)	0.076
No	11 (91.7)	25 (65.8)	

PICU: Pediatric intensive care unit

period. Hospitalizations most frequently occurred in winter (17 cases, 34%), and secondly in spring (14 cases, 28%). Viral agents were detected on the nasopharyngeal swab of 2 cyanotic patients (16.7%) and 7 acyanotic patients (18.4%). RSV was the most frequent viral agent which was isolated in totally 5 patients diagnosed with PDA, VSD+ASD, operated DORV and isolated VSD, (2 patients had viral co-infections including RSV determined below). Bocavirus was found in 2 cases diagnosed with VSD and DORV, and influenza B was found in 1 case diagnosed with VSD. In 3 other cases, viral co-infections found were influenza A and Rinovirus in 1 case diagnosed with TOF; RSV and Parainfluenza virus in 1 case diagnosed with PDA and RSV; Parainfluenza, Rhinovirus and Human Metapneumonia virus in 1 other case diagnosed with VSD. RSV was not seen in the cyanotic group ( $p=0.305$ ). Three of 5 RSV infected patients (60%) were hospitalized in winter. Therefore, these patients received incomplete RSV prophylaxis. Similarly, 5 of the total 9 viral agent (+) patients (55.6%) were hospitalized in winter (Table II). All of the RSV infected patients were under 12 months of age. Two of them had extracardiac risk factor (Down syndrome and prematurity with bronchopulmonary dysplasia). One (8.3%) of the cyanotic patients who was a two-year-old boy with tracheostomy cannula and home ventilator had bacterial LRTI. The agent was Haemophilus influenzae. Four (10.5%) of the acyanotic patients had also had bacterial LRTI. These were respectively 2,7,2 and 54 months old, and the agents were Stenotrophomonas maltophilia, Klebsiella pneumoniae, Pseudomonas aeruginosa. The second and fourth patients had neurological sequelae and cerebral palsy. Unfortunately, the first patient have been lost died in the pediatric intensive care unit (PICU) after surgery of severe AC with respiratory system complications. One of the cyanotic patients who was aged 3 months, diagnosed with DORV and admitted to the PICU died due to respiratory failure. He had had no extracardiac problems and no viral or bacterial agents were detected. Thirteen of 38 (34.2%) acyanotic patients needed PICU admission ( $p=0.076$ ), 2 of them died because of acute Respiratory Distress syndrome aged 2 months and 2 years, and they had had no extracardiac problems either.

Viral agent frequency related season			
Viral agent		Frequency (n)	%
(+)	Winter	5	55.6
	Summer	1	11.1
	Spring	3	33.3
	Autumn	0	0
	Total	9	100.0
(-)	Winter	12	29.3
	Summer	7	17.1
	Spring	11	26.8
	Autumn	11	26.8
	Total	41	100.0

The first patient had a bacterial agent, Stenotrophomonas maltophilia. Viral and bacterial agents were not found in the second patient. There was no statistically significant difference between the two groups (Table I). When compared for hospitalization times, there was no significant difference between the type of CHD, season, age and viral agent (Table III).

## Discussion

LRTI are defined in the International Classification of Diseases as infections that affect airways below the epiglottis (5). Some children have predisposing risk factors such as prematurity, CHD, chronic lung disease, immune disorders, being below 5 years of age, environmental smoke exposure, oropharyngeal incoordination with Aspiration syndrome (6-9). Also children with HS-CHD with congestive heart failure are more at risk for LRTI causing mortality and morbidity (10-12). Incidence of CHD differs for populations and the most common type of CHD is VSD (1). Some kind of CHD which leads to increased pulmonary flow (e.g. VSD, PDA) or CHD with desaturation (e.g. TOF, DORV, truncus arteriosus) carries a higher risk of recurrent respiratory tract infections and increased frequency of hospitalizations (2). According

	Hospitalization time (day) Mean $\pm$ standart deviation Median (minimum-maximum)	p value
<b>CHD</b>		
Cyanotic	12.68 $\pm$ 11.909 9.0 (4-53)	0.239
Acyanotic	13.53 $\pm$ 7.357 12.0 (3-30)	
<b>Season</b>		
Winter	12.35 $\pm$ 8.046 10.0 (3-30)	0.578
Summer	15.5 $\pm$ 8.602 15.5 (5-26)	
Spring	10.78 $\pm$ 4.838 10.0 (4-21)	
Autumn	16.18 $\pm$ 13.526 15.0 (4-53)	
<b>Age</b>		
<12 months	14.69 $\pm$ 10.048 13.0 (3-53)	0.114
$\geq$ 12 months	10.47 $\pm$ 5.535 9.0 (4-23)	
<b>Respiratory viral panel</b>		
Agent +	9.44 $\pm$ 5.228 9.0 (3-20)	0.119
Agent -	14.09 $\pm$ 9.412 12.0 (4-53)	

CHD: Congenital heart disease

to a review of 38 studies, especially HS-CHD patients with pulmonary congestion before the age of 2 are more likely to be hospitalized with severe RSV infections (13). In our study, similar to the literature, acyanotic CHD, especially VSD was the most frequent patient group that needed hospitalization for LRTI. We saw that children with pulmonary congestion were more at risk for PICU admission. Acute respiratory tract infections of childhood are usually seen before the age of 2. The American Academy of Pediatrics has included children with HS cyanotic CHD and acyanotic CHD, bronchopulmonary dysplasia, and prematurity in the high risk group for RSV infection, extended the age limit to 2 years, and recommended RSV prophylaxis (14). According to one study from China with 2721 hospitalized children those who were under 6 months old and who had CHD carried a higher risk of severe RSV disease (15). In our study 68% of the patients were younger than 12 months, 84% were younger than 24 months of age, similar to the literature (16-17). Medrano et al. (3) carried out CIVIC Epidemiologic Study with children who had HS-CHD, and found significant associated risk factors such as previous respiratory disease, incomplete immunoprophylaxis against RSV, Di George syndrome, Down syndrome, cardiopulmonary bypass, and siblings aged less than 11 years old. In the study, the most commonly identified infectious agent was RSV, like in our study. Also one study from Turkey by Ozyurt et al. (18) revealed that children having CHD without RSV prophylaxis are more at risk for complicated LRTI, LRTI-related hospitalization, and intensive care unit admission. They also stated that patients with prophylaxis in the presence of siblings under the age of 12 and with congestive heart failure suffer from LRTI-related hospitalizations (18). Down syndrome with or without CHD is a risk factor leading to mortality or hospitalization (4). Similarly, in our study some patients had extracardiac risk factors and 4 of these patients were in early postoperative period after cardiopulmonary bypass (7 patients with Down syndrome and 1 patient with Di George syndrome, 7 patients with prematurity, 1 patient with congenital adrenal hyperplasia, 16/50). Additionally, in our study all of the patients had at least 1, and 68% of the patients had 2 or more school-aged siblings. As we think that school-aged children act as a carrier, living with school-aged siblings increases the risk of LRTI and also the morbidity of LRTIs. Passive smoking or environmental smoke exposure is also a risk factor causing recurrent LRTI (19,20). But in contrast to the literature, in our study more than half of the patients had not been exposed to cigarette smoke. Hospitalization most commonly was seen in winter (34% of all hospitalizations) but there was no significant difference regarding the hospitalization time of the patients in our study (Table II).

### Study Limitations

The most important limitation was the number of patients in the study.

## Conclusion

In this study we report children with CHD, hospitalized in a single center having been diagnosed with LRTI; the demographic variables, risk factors, infectious agents causing mortality and morbidity in the light of the literature. To prevent these risk factors more studies must be done.

### Ethics

**Ethics Committee Approval:** This study was approved by the Ege University Faculty of Medicine Ethics Committee (approval number: 14-11/11).

**Informed Consent:** After being informed of the purpose and content of the study by the doctor and having read the information for patients, all the parents gave written informed consent.

**Peer-review:** External and internal peer-reviewed.

### Authorship Contributions

Surgical and Medical Practices: E.K., Y.Ö.Ş., Z.Ü.T., Concept: Z.Ü.T., Design: Y.Ö.Ş., Z.Ü.T., Data Collection or Processing: E.K., Y.Ö.Ş., Analysis or Interpretation: E.K., Literature Search: Y.Ö.Ş., Writing: Y.Ö.Ş., Z.Ü.T.

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