Original Investigation / *Özgün Araştırma*

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# The Relationship Between Viruses and Clinical Findings in Hospitalized Children Diagnosed with Acute Lower Respiratory Tract Infection

## Akut Alt Solunum Yolu Enfeksiyonu Tanısı ile Hastaneye Yatırılan Çocuklarda Viral Etkenler ve Klinik ile İlişkisi

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**Abstract**

**Objective:** In this retrospective study, we aimed to identify viral agents in children hospitalized with ALRTI and to show the relationship between viral agents and clinical characteristics.

**Material and Methods:** Two hundred and fifty five children (55.7% male) who were diagnosed with ALRTI and hospitalized between March 2016 and February 2017 were included in the study. Clinical characteristics of the patients who were examined to detect respiratory tract viruses with PCR analysis in nasopharyngeal swab samples were evaluated by using medical records. The patients were divided into three groups according to their age: under two years old, between 2-6 years old, and between 6-18 years old. Newborns were not included in the study.

**Results:** Two hundred and three patients (79.6%) were under two years old. Thirty eight patients (14.9%) were aged 2-6 years, and 14 patients (5.5%) were aged 6-18 years. Among the age groups, male gender was significantly higher in the patients who were under two years old (p= 0.018). There was no significant difference hospitalization between the age groups and the genders in the clinic of pediatrics and the intensive care unit (p= 0.34). A single virus was detected in 158 patients (62%), and more than one viral agent was detected in 35 patients (13.7%). The most frequent virus was RSV (31.8%). However, RSV was not detected in any patient between the ages of 6-18. Respiratory syncytial virus was followed by iRV (11.8%), iMPV (5.1%) and iCoV (3.9%), respectively. No significant difference was found between the clinical findings of the viruses. Twenty four point two percent of the patients had no virus that

**Öz**

**Giriş:** Bu retrospektif çalışmada ASYE nedeniyle hastaneye yatırılan çocuklarda viral etkenleri tespit etmeyi ve etkenlerle klinik arasındaki ilişkiyi göstermeyi amaçladık.

**Gereç ve Yöntemler:** Çalışmaya Mart 2016 ile Şubat 2017 tarihleri arasında ASYE tanısı alan ve hastaneye yatırılan 255 çocuk hasta (%55.7'si erkek) dahil edildi. Solunum yolu virüslerini tespit etmek amacıyla nazofarengeal sürüntü örneklerinden PZR analizi yapılan hastaların klinik özellikleri dosya kayıtları incelenerek değerlendirildi. Hastalar yaşlarına göre iki yaş altı, 2-6 yaş arası ve 6-18 yaş arası olmak üzere üç gruba ayrıldı. Yenidoğanlar çalışmaya dahil edilmedi.

**Bulgular:** İki yüz üç hasta (%79.6) iki yaşın altındaydı. Otuz sekiz hasta (%14.9) 2-6 yaş, 14 hasta (%5.5) 6-18 yaş arasındaydı. Yaş grupları arasında iki yaş altı hastalarda erkek cinsiyet anlamlı olarak daha yüksek bulundu (p= 0.018). Pediyatri kliniği ve yoğun bakım ünitesinde yatış durumu açısından yaş grupları arasında anlamlı farklılık yoktu (p= 0.34). Yüz elli sekiz hastada (%62) tek viral etken, 35 hastada (%13.7) birden fazla viral etken tespit edildi. En sık saptanan virüs RSV (%31.8) idi. Ancak 6-18 yaş arasında hiçbir hastada RSV yoktu. Respiratuvar sinsityal virüsü sırasıyla iRV (%11.8), iMPV (%5.1) ve iCoV (%3.9) izledi. Virüslerin klinik bulguları arasında anlamlı farklılık bulunmadı. Hastaların %24.2'sinde PZR ile viral etken saptanmadığı görüldü. Virüs negatif hastalara kıyasla nazofarengeal sürüntü örneklerinde en az bir virüs bulunan hastaların hastanede yatış süreleri daha uzundu.

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was detected with PCR test. Hospitalization duration was longer in virus-negative patients compared to patients who had at least one virus in their nasopharyngeal swab samples.

**Conclusion:** Most respiratory viruses may be detected with PCR analysis in nasopharyngeal swab samples. However, detecting to all respiratory viruses may not always be possible. In the present study hospitalization duration in virus-negative patients was longer than patients with at least one viral agent suggests that more comprehensive studies are needed.

**Keywords:** Child, polymerase chain reaction, respiratory tract infections, virus

**Sonuç:** Nazofarengeal sürüntü örneklerinin PZR analiziyle solunum yolu virüslerinin büyük bir bölümü tespit edilebilir. Ancak tüm virüslerin gösterilmesi her zaman mümkün olmayabilir. Çalışmamızda virüs negatif hastaların hastanede yatış süresinin en az bir virüs tespit edilen hastalara göre daha uzun olması daha kapsamlı çalışmalara ihtiyaç olduğunu düşündürmektedir.

**Anahtar Kelimeler:** Çocuk, polimeraz zincir reaksiyonu, solunum yolu enfeksiyonları, virüs

## Introduction

Acute lower respiratory tract infection (ALRTI) is one of the most common infections of childhood. Clinical manifestations can range from mild, cold-like symptoms to life-threatening symptoms (1). It is one of the leading causes of hospitalization in infants and young children worldwide. Respiratory syncytial virus (RSV) is the most common virus detected by polymerase chain reaction (PCR) in children under the age of two who are hospitalized with ALRTI. In addition, human rhinovirus (hRV), human parainfluenza virus (hPIV), influenza virus, adenovirus, human metapneumovirus (hMPV), human bocavirus (hBoV), and many other viruses have been increasingly detected both in the community and in hospitalized patients (2). Understanding the causative agents of ALRTI can provide insight into patient management and clinical course, and may guide treatment (3).

The aim of this retrospective study was to examine the viral agents that cause ALRTI and their clinical characteristics in hospitalized children.

## Materials and Methods

Patients diagnosed with ALRTI and hospitalized between March 2016 and February 2017 were included in the study. Patients were divided into two groups as diagnosed with acute bronchiolitis and pneumonia according to medical records. Patients under the age of two with mild fever and wheezing, sibilant rhonchi and rals on auscultation, normal or slightly elevated white blood cell count in laboratory tests, and increased aeration and/or peribronchial infiltration on chest X-ray were diagnosed with acute bronchiolitis (4). Patients with consolidation on chest X-rays were defined as pneumonia (5). Patients older than two years and admitted to the hospital for the first time with a wheezing episode were evaluated as virus-induced wheezing (6).

Patients' age, gender, birth weight (birth weight <2700 gram was defined as low birth weight), week of birth (gestational week <37 weeks was defined as prematurity), history of inhaled salbutamol treatment, family history of asthma, cigarette smoke exposure, and history of underlying chronic diseases were recorded.

Complete blood count, C-reactive protein (CRP) tests, and posteroanterior (PA) chest radiographs of the patients were obtained from the hospital records. The results of reverse transcription polymerize chain reaction (PCR) testing of nasopharyngeal swab samples collected with disposable sterile DNA sampling kits and analyzed in the General Directorate of Public Health's reference laboratory were examined.

The patients' clinical features such as fever, tachypnea, tachycardia, hypoxia, oxygen support treatment methods, need for intensive care and duration of hospital stay were evaluated. Free oxygen therapy with mask or nasal cannula, non-invasive [high flow nasal cannula (YANC), nasal continuous positive airway pressure (DPHB)] ventilation and invasive mechanical ventilation in patients with oxygen saturation <94% and/or in need of respiratory support stuations were recorded.

The monthly distribution of viruses detected by PCR from nasopharyngeal swab samples was examined.

The length of hospital stay [pediatric clinic and intensive care unit (ICU)] of the patients was recorded.

Ethics committee approval was received from Ankara Training and Research Hospital Ethics Committee (No: 2019/734).

SPSS 15.0 for Windows software was used for statistical analysis. Descriptive statistics were given as numbers and percentages for categorical variables, and median and interquartile range for numerical variables. >2 independent group comparisons of numerical variables were done using the One Way ANOVA test when the numerical variables met the normal distribution condition, and with the Kruskal Wallis test when they did not meet the normal distribution condition. Subgroup analyses were performed with the Mann-Whitney U test and interpreted with Bonferroni correction in the nonparametric test. The ratios in the groups were found using the Chi-square test. Statistical alpha significance level was set at $p< 0.05$.

## Results

Of 450 patients diagnosed with ALRTI, 149 patients were excluded from this study who had no nasopharyngeal swab samples due to technical reasons and 46 patients were exclud-

ed who had incomplete medical records. A total of 255 (55.7% male) patients were included in the study. The mean age was 18.57 months (minimum 0.39, maximum 213, standard deviation 31.28). Two hundred and three patients (79.6%) were under two years old. Thirty-eight patients (14.9%) were aged 2-6 years, and 14 patients (5.5%) were aged 6-18 years. Among the age groups, the male gender was significantly higher in the patients who were under two years old (p= 0.018).

Thirty-four (13.3%) patients had a history of prematurity, 43 (16.1%) patients had low birth weight, and 98 (38.4%) patients had a history of born with cesarean section (C/S). The mean birth weight of the patients was 3047 ± 628 grams (min. 770, max. 5000 gram), and the median week of delivery was 39 weeks (min. 24, max. 42 weeks). Sixty-five patients (25.5%) received incubator care for any reason during the neonatal period. Sixty-seven patients (26.3%) had a history of ALRTI, and 62 patients (24.3%) had a history of inhaled salbutamol treatment.

Three patients (1.2%) had a mother with asthma, one patient (0.4%) had a father with asthma, and 11 patients had brother/sister with asthma (4.3%). Twenty-four patients (9.4%) had exposure to passive smoking.

Ninety-five patients (37.3%) were diagnosed with acute bronchiolitis, 154 patients (60.4%) with pneumonia. Six patients (2.4%) were considered to have virus-induced wheezing. In terms of age groups, 108 (70.1%) of the patients diagnosed with pneumonia were under the age of two, 32 (20.1%) were 2-6 years old, and 14 (9.1%) were 6-18 years old.

Table 1 shows the clinical and laboratory findings based on the patients' age groups. There was no significant difference between gender and age groups in terms of hospitalization in the pediatric ICU (p= 0.34).

At least one virus was detected in 193 (75.7%) of 255 nasopharyngeal swab samples. Eighty-one (31.8%) were positive for RSV only, 30 (11.8%) were positive for hRV only, 13 (5.1%) were positive for hMPV only, and 10 (3.9%) were positive for human coronavirus (hCoV) only. There was not any virus in 62 (24.2%) samples, and 35 (13.7%) had more than one virus. Respiratory syncytial virus was detected in 48 patients (31.3%) and hRV in 14 (9.15%) patients who were diagnosed with pneumonia. In patients diagnosed with acute bronchiolitis RSV was detected in 32 (33.3%) and hRV was detected in 13 (13.54%). The respiratory syncytial virus was the most frequently detected virus in nasopharyngeal swab samples. Identification and frequency of the viruses detected in patients are shown in Table 2.

Viral agents were detected in 161 patients (79.8%) under the age of 2, in 28 patients (73.6%) between the ages of 2-6, and in 3 patients (21.4%) between the ages of 6-18. The respiratory syncytial virus was found to be the most common viral agent in patients under the age of two (p< 0.001). However, RSV was not detected in any patient between the ages of 6-18. In this age group, the absence of virus in nasopharyngeal swab samples was statistically more common (p< 0.001). Viral agents according to age groups are shown in Table 3.

Rhonchi were found less frequently in physical examinations in patients aged 6-18 years (p= 0.001). On admission, the oxygen saturation was <94% in 34 patients (13.3%). 187 patients (73.3%) received free oxygen therapy, 66 patients (25.9%) received non-invasive ventilation support with HFNC and/or CPAP and two patients (0.8%) received invasive mechanical ventilation. There was no statistically significant difference between the form of respiratory support and age,

**Table 1.** Clinical and demographic characteristics of patients with acute lower respiratory tract infection based on age groups

| | <2 years | 2-6 years | 6-18 years | p |
|---|---|---|---|---|
| Birth week | 39 (38-39) | 39 (38-39) | 39 (38-39) | 0.238 |
| Birth weight (grams) | 3000 (2725-3500) | 3140 (3000-3613) | 3000 (2125-3550) | 0.172 |
| Fever (°C) | 37 (36-38) | 37 (36-38) | 37 (36-38) | 0.747 |
| Tachypnea, n (%) | 35 (17.2) | 14 (36,8) | 10 (71.4) | ***0.01*** |
| $SaO_2$ (%) | 96 (95-98) | 97 (93-98) | 96 (93-97) | 0.663 |
| Tachycardia, n (%) | 153 (75.4) | 32 (84.2) | 10 (71.4) | ***0.011*** |
| Leukocytes ($x10^3/mm^3$) | 11.8 (9.63-15.2) | 13.05 (9.45-18.5) | 10.7 (6-27.02) | 0.663 |
| PICU, n (%) | 4 (2-7) | 5 (2-7) | 35 (6-63) | 0.46 |
| Pediatric clinic, n (%) | 5 (4-7) | 4 (3-6) | 5 (3-9) | 0,183 |
| HFNC, n (%) | 3 (2-5) | 9 (5-13) | 3 (2-4) | 0.069 |
| CPAP, n (%) | 4 (3-6) | 4 (3-7) | - | 0.777 |

Numerical values are given as median (interquartile).

CPAP: Continuous positive airway pressure, HFNC: High flow nasal cannula, PICU: Pediatric intensive care unit, $SaO_2$: Oxygen saturation

**Table 2.** Identification and frequency of the viruses detected in patients with acute lower respiratory tract infections

| | Total, n (%) | Single agent, n (%) | Other*, n (%) | p |
|---|---|---|---|---|
| RSV A/B | 99 (38.8) | 81 (51.3) | 18 (18.6) | **<0.001** |
| hRV | 49 (19.2) | 30 (19) | 19 (19.6) | 0.906 |
| hMPV | 18 (7.1) | 13 (8.2) | 5 (5.2) | 0.352 |
| hCoV (OC43. HKU1. NL63. 229E) | 15 (5.9) | 10 (6.3) | 5 (5.2) | 0.699 |
| Parainfluenza virus (2. 3. 4) | 19 (7.5) | 9 (5.7) | 10 (10.3) | 0.173 |
| Adenovirus | 13 (5.1) | 5 (3.2) | 8 (8.2) | 0.085 |
| hBoV | 10 (3.9) | 6 (3.8) | 4 (4.1) | 1.000 |
| Influenza virus B | 2 (0.8) | 3 (2) | 1 (1) | - |
| Influenza virus A (H3N2) | 1 (0.4) | 1 (0.6) | 1 (1) | - |
| Enterovirus | 1 (0.4) | - | 1 (1) | 0.38 |

*Indicates the number of patients with other viruses.
hBoV: Human bocavirus, hCoV: Human coronavirus, hMPV: Human metapneumovirus, hRV: Human rhinovirus, RSV: Respiratory syncytial virus.

**Table 3.** The frequency of the viruses detected in patients with acute lower respiratory tract infections based on age groups

| | <2 years (n= 203) | 2-6 years (n= 38) | 6-18 years (n= 14) | p |
|---|---|---|---|---|
| RSV A/B | 94 (46.3) | 5 (13.2) | 0 | ***<0.001*** |
| hRV | 34 (16.7) | 13 (34.2) | 2 (14.3) | ***0.038*** |
| hMPV | 17 (8.4) | 1 (2.6) | 0 | 0.378 |
| hCoV (OC43. HKU1. NL63. 229E) | 14 (6.9) | 1 (2.6) | 0 | 0.584 |
| Parainfluenza virus (2. 3. 4) | 16 (7.9) | 2 (5.3) | 1 (7.1) | 0.901 |
| Adenovirus | 10 (4.9) | 3 (7.9) | 0 | 0.512 |
| hBoV | 6 (3.0) | 4 (10.5) | 0 | 0.109 |
| Influenza virus type-A (H3N2) | 1 (0.5) | 1 (2.6) | 0 | 0.5 |
| Influenza virus type-B | 1 (0.5) | 0 (0) | 0 | - |
| Enterovirus | 0 | 1 (2.6) | 0 | 0.210 |
| Multiple agents | 31 (15.3) | 4 (10.5) | 0 | 0.227 |
| Virus-negative | 41 (20.2) | 10 (26.3) | 11 (78.6) | ***<0.001*** |

Group data, n (%).
hBoV: Human bocavirus, hCoV: Human coronavirus, hMPV: Human metapneumovirus, hRV: Human rhinovirus, RSV: Respiratory syncytial virus.

gender, and clinical diagnosis (p values 0.085, 0.26, 0.27, respectively).

Table 4 shows the demographic, clinical, and laboratory findings of patients who had single infection with RSV, hRV, hMPV, and hCoV. Patients with hRV were older than others (p< 0.001).The absolute neutrophil count (ANC) was found to be higher in patients with hRV than in patients with RSV and hCoV (p= 0.005). The eosinophil count was lower in patients with RSV than those with hRV (p= 0.027). A history of low birth weight was more common in patients with hCoV compared to patients with respiratory syncytial virus and hRV (p= 0.017). There was no significant difference between viral agents and the length of hospital stay (p= 0.9 for the ICU, p= 0.5 for the pediatric clinic). Duration of hospital stay was longer in patients who had no virus compared to patients with at least one virus in nasopharyngeal samples (p= 0.004).

Nine percent of the patients had comorbidities such as congenital heart disease, asthma, cerebral palsy, neuromuscular disease, and hydrocephalus. There was no statistically significant difference in the rates of hospitalization ICU between patients with and without comorbidities (p= 0.110). The length of ICU stay in patients with comorbidities was higher than those without comorbidities (p= 0.021). The virus detection rate was lower in patients with comorbidities (p= 0.025). Respiratory syncytial virus was detected less frequently in patients who had comorbidities (p= 0.036).

When compared with monthly distribution of viral agents, there was a statically significant that RSV was more frequent in January and February (p< 0.001). Hospitalization rate for ALRTI was high in January (21.5%) and February (20%), whereas it was lowest (0.8%) in July (Figure 1).

**Table 4.** Demographic, clinical, and laboratory characteristics of patients with acute lower respiratory tract infection caused solely by RSV A/B, hRV, hCoV, and hMPV

| | RSV A/B (n= 81) | hRV (n= 30) | hCoV (n= 10) | hMPV (n= 13) | p |
|---|---|---|---|---|---|
| Birth week (<37 weeks)* | 10 (13.2) | 8 (29.6) | 1 (10) | 4 (30.8) | 0.128 |
| Birth weight (<2700 grams)* | 11 (14.5) | 11 (40.7) | 2 (20) | 5 (38.5) | ***0.017*** |
| Age (months)** | 5 (2-8.5) | 21 (6.5-35.5) | 6 (1-14.25) | 7 (5-10) | ***<0.001*** |
| Family history of asthma* | 3 (3.9) | 3 (10.7) | 0 (0) | 2 (15.4) | 0.179 |
| Cigarette smoke exposure* | 10 (13) | 0 (0) | 0 (0) | 2 (15.4) | 0.103 |
| Hypoxia ($SaO_2$ < 94)* | 6 (10) | 7 (29.2) | 2 (28.6) | 2 (15.4) | 0.100 |
| Tachycardia | 59 (72.8) | 24 (80) | 7 (70) | 13 (100) | 0.464 |
| Tachypnea | 19 (23.5) | 9 (30) | 1 (10) | 3 (23.1) | 0.383 |
| Abnormal X-ray* | 46 (56.8) | 17 (56.7) | 5 (50) | 9 (69.2) | 0.804 |
| Leukocytes ($x10^3/mm^3$)** | 11.5 (9.5-14.07) | 12.6 (9.2-17.5) | 11.15 (9-17.02) | 13.1 (10.05-14.3) | 0.629 |
| ANC ($x10^3/mm^3$)** | 5.3 (3.2-7.4) | 7.1 (4.9-13.3) | 3.2 (2.1-7.9) | 6 (4.9-9.1) | ***0.006*** |
| ALC ($x10^3/mm^3$)** | 4.7 (3.1-6.5) | 3.4 (1.7-5.9) | 4.9 (4.3-6.2) | 4.4 (2.6-6.5) | 0.350 |
| Eosinophil ($x10^3/mm^3$)** | 10 (0-130) | 100 (7.5-325) | 100 (0-525) | 0 (0-245) | ***0.027*** |
| CRP (mg/L)** | 1 (0-3) | 1 (0-2) | 0.5 (0-3.25) | 2 (1-3.5) | 0.503 |
| ICU (number of hospitalization days)** | 3 (2-6.75) | 3 (1.5-5.5) | 4.5 (1-8) | 3 (2-10) | 0.910 |
| Pediatric clinic (number of hospitalization days)** | 5 (4-6.5) | 4.5 (2.7-6.25) | 5 (3.75-6.25) | 6 (4.5-8.5) | 0.539 |
| HFNC (number of days)** | 0 (0-0) | 0 (0-0) | 0 (0-0) | 0 (0-3) | 0.198 |

*Numerical values, n (%)
**Numerical values median (interquartile)
ANS: Absolute neutrophil count, ALS: Absolute lymphocyte count, CRP: C-reactive protein, hCoV: Human coronavirus, HFNC: High flow nasal cannula, hMPV: Human metapneumovirus, hRV: Human rhinovirus, ICU: Intensive care unit, RSV: Respiratory syncytial virus, $SaO_2$: Oxygen saturation.

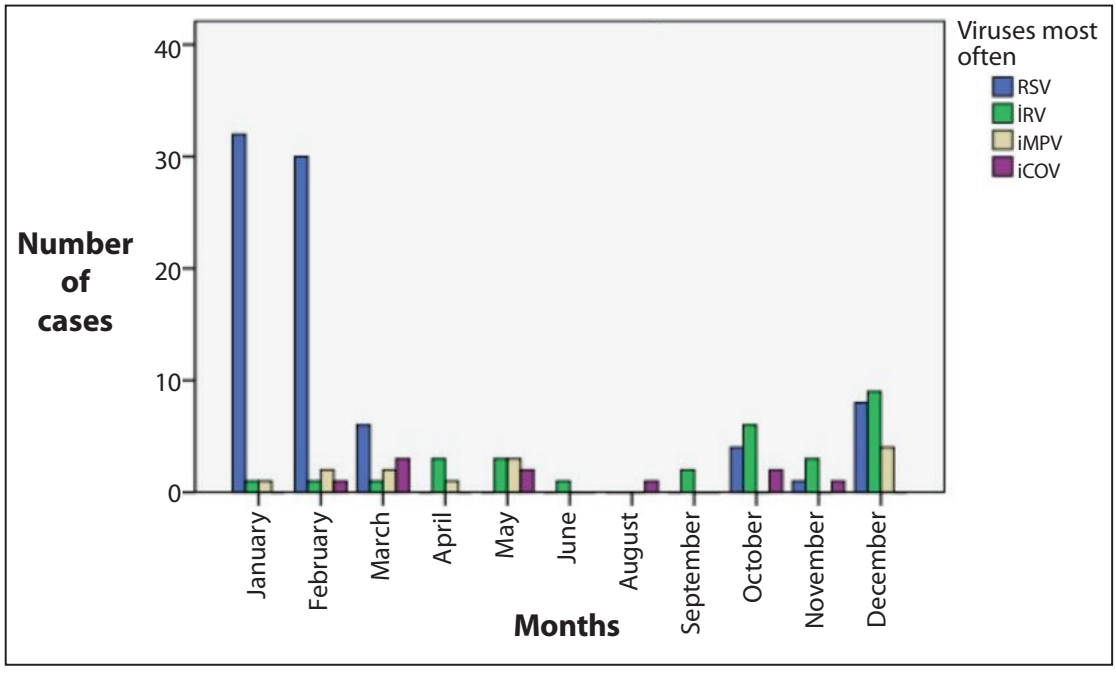


**Figure 1.** Range of viruses (RSV, IRV, iMPV, iCoV) by months.

## Discussion

In the present retrospective study, RSV was the most common virus in 38.8% of our patients, in which we used PCR that is one of the methods to detect causative agents of childhood ALRTI. Respiratory syncytial virus was detected more frequent in children under the age of two, and it was not found in any of the patients aged 6-18. Male gender was significantly hig-

her in patients under the age of two. There was no significant difference between viral infections in terms of physical examination findings (ral, rhonchus, retraction), length of hospital stay (ICU and pediatrics clinic), oxygen therapy, invasive and non-invasive mechanical ventilation needs. Hospitalization stay in ICU was longer in patients who had comorbidities. In addition, detection rate of a viral agent was lower, and RSV was less frequent in this group. Thirteen point seven percent of patients had more than one virus in nasopharyngeal swab samples. The majority of these patients were under the age of two (88.6%). There was no significant difference between the clinical findings of the patients who had a single virus and the patients with more than one virus.

The respiratory syncytial virus is the most important cause of viral ALRTI in infants and children (5). Globally, it is estimated that there are 34 million new cases of ALRTI caused by RSV in children under the age of five, 3-4 million of these patients are hospitalized, and 199 thousand patients die, mostly in developing countries (6). Studies have reported hRV as the second most common cause of ALRTI (3,7-9). Respiratory tract viruses may differ according to different regions, wheather conditions, and indoor crowding (10). In a study from Iran, patients diagnosed with respiratory tract infections were divided into age groups of <2 years, 2-5 years, and 6-15 years; RSV was the most common virus (42%) in patients under two years of age. However, no statistically significant difference was found in the distribution of viral agents between age groups (11). In a study conducted in Russia, it was reported that RSV and hMPV were more common in children under one year of age than in children aged 1-3 years, RSV was less common in school-age children, and ALRTI caused by influenza virus were more common (12). In a study from China it was reported that RSV as the second most common agent after *M. pneumoniae* in patients aged 5-14 years (13). In our study, the most common virus was RSV under two years of age, and hRV between 2-6 years of age. Although data on ALRTI caused by RSV between the ages of 6-18 are limited, recurrent RSV infections can be seen in older children and adults especially in contact with young children. It mostly presents as upper respiratory tract infections (14). In addition, *S. pneumoniae* is the most common cause of ALRTI between the ages of 6-9 and *M. pneumoniae* is the most common cause of ALRTI in patients aged >10 years. Virus-induced ALRTI are less common (5). Respiratory syncytial virus was not detected in any of the patients in our study between the ages of 6-18, which is consistent with the published data. In this age group, hRV was detected in two patients, parainfluenza virus was detected in one patient and there was no virus in 78.6% of patients.

In our study, although the most common respiratory viral pathogens were detected by use PCR, there was no virus in 24.3% of patients. In the present study only viral agents were detected by use PCR and bacterial agents could not detect, so celar differantion of viral vs. bacterial ALRTI could not be made. However, the absence of virus in PCR test does not always mean that patients are free of viral agents, as PCR tests may not detect all respiratory viruses.

In nasopharyngeal samples, both etiological and non etiological viruses can be detected using by PCR (16). Viruses have been detected in the respiratory tracts of children who show no signs of an ALRTI (1,15). Even though the presence of hRV in children's respiratory tracts even two weeks after the resolution of symptoms raises questions about hRV positivity in PCR tests, hRV has been identified as a causative agent for ALRTI (8). In our study, hRV was detected as the only viral agent in 11.8% of the patients. Since these patients were symptomatic and required hospitalization, hRV was accepted as the causative agent.

One third of children hospitalized for ALRTI have more than one virus. Respiratory syncytial virus+hRV is the most commonly reported co-infection according to the data from Genetics, Vitamin D, and Respiratory Infections Research Network (www.gendres.org) (GENDRES), while RSV+hBoV and influenza+hBoV are the most frequently reported co-infections in the UK data. This disparity was thought to be due to the 2009 influenza pandemic in the United Kingdom. Co-infections were most common in children aged 12-24 months (8). Another study found that 70% of severe bronchiolitis cases caused by RSV were also infected with hMPV, and that the clinical course in cases of RSV+hMPV co-infection could be severe (17). In population-based and case-control studies of hospitalized children, however, hMPV+RSV co-infection is uncommon (8). In our study, the most common co-infection in patients was RSV+hRV, consistent with GENDRES data. More than one viral agent was detected most frequently in patients under the age of two, particularly those under the age of 12 months. The most frequently detected viruses in co-infections were RSV, hRV, and parainfluenza virus, respectively. Fourteen point two percent of the patients with co-infections were admitted to ICU. In addition, hMPV+RSV co-infection was present in three patients (1.2%). There was no difference in clinical findings and duration of hospital stay in these patients.

Respiratory tract viruses may differ according to different regions, climatic and seasonal conditions (10). According to a recent study, RSV, the most common causative agent, peaked between December and February, while hMPV, the second most common causative agent, peaked in January (11). Another study showed that the most common causative agent, RSV, peaked in December and January, while the second most common, hRV, peaked twice, once in January and once in October-November (3). In our study, we found that RSV was most common in January and February; the second most common virus, hRV, in October and December, and the third most com-

mon virus, hMPV, in December and February. Forty seven point eight percent of the patients under the age of two were hospitalized due to ALRTI in January and February when RSV is more common.

Our retrospective study is insufficient to predict the frequency of viral agents in patients with ALRTI who have milder symptoms and do not require hospitalization, since we only studied viral agents in patients with ALRTI who have clinical findings that are severe enough to require hospitalization. The absence of any causative agent in 24.3% of the patients can be considered as a result of the inability to detect both bacterial agents and all other respiratory tract viruses since the PCR analysis in the study could detect a limited number of viral pathogens. However, with respiratory PCR analysis, it is possible to detect rare viruses, predict possible epidemics, and prevent unnecessary antibiotic use.

## Conclusion

In this retrospective study, while RSV was found to be the most common viral agent for ALRTI in children under two years of age, it was not detected in any patient aged 6-18 years. Male gender was more common in patients younger than two years of age. Patients with no viral agents had a longer hospital stay. PCR, which is one of the methods used for the detection of viral agents in nasopharyngeal swab samples, can show the majority of the agents. It can be effective in distinguishing between viral and bacterial ALRTI in most patients and preventing unnecessary antibiotic use. However, it should be noted that not all respiratory tract viruses can be demonstrated with PCR. Therefore, more comprehensive studies are needed.

**Ethics Committe Approval:** Ethical approval for this study was obtained from the Ethics Committee of Ankara Training and Research Hospital (Decision No: 2019/734).

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