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Respiratory viruses in hospitalized children with acute respiratory infections at 2019-2020 autumn-winter season: A single-center experience before COVID-19 pandemic

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Abstract

The aim of this study is to determine the causative respiratory viruses (RVs) in hospitalized children due to acute respiratory tract infections (RTIs) in the 2019-2020 fall-winter season, before the COVID-19 pandemic, examine the clinical and laboratory findings, discuss the prevention strategies during the ongoing pandemic process, and contribute to the literature by providing data just before the pandemic. Aged between one month-18 years of patients who were admitted to Sivas Cumhuriyet University Hospital and hospitalized due to acute RTIs between September 1, 2019, and March 1, 2020, and had a RVs multiplex PCR panel were analyzed retrospectively. 139 patients were evaluated. At least one viral pathogen was detected in 105 (75.5%) patients. 5 patients (3.59%) had co-infection. The most common viruses detected were Influenza A (H1N1) (21.8%), Influenza B (20.9%), Rhinovirus (RV) (18%) and, Respiratory Syncytial Virus (RSV) (17.3%). RSV was the most common viral agent under the age of 1. 52 patients (37.4%) were followed up in Pediatric Intensive Care Unit (PICU), and the most common viral pathogens isolated in PICU were RSV (17.3%), RV (17.3%) and Bocavirus (HBoV)(9.6%). RV and HBoV patients needed high levels of oxygen and respiratory support. Unnecessary antibiotic use and morbidity can be reduced by detecting the viral agent in the early period with the PCR method. RSV prophylaxis and influenza vaccination should be continued uninterruptedly for children at risk groups during the COVID-19 pandemic process.

Keywords: Acute respiratory infection, real-time PCR, respiratory viruses, RSV, influenza, children, COVID-19

Introduction

Respiratory infections are one of the leading causes of infection-related morbidity and mortality in children worldwide [1]. Viruses are the most common cause of respiratory tract infections (RTIs) in children [2]. Although mild and self-limiting infections are seen most frequently, the clinical picture may vary according to the age groups of the cases, the season, the presence of the underlying disease, and the location of the infection. Severe pictures such as multi-organ failure can also be seen [3].

The most common causes of respiratory tract infections in children are Respiratory Syncytial Virus (RSV), Rhinovirus (RV), and seasonal influenza viruses, which trigger epidemics most often during the winter months. Human metapneumovirus (hMPV), parainfluenza virus (PIV), human bocavirus (hBoV), human coronavirus (hCoV) 229E, OC43, and NL63 are other viruses that cause respiratory infections in children and adults. The etiology of many viruses can now be determined quickly and easily using modern molecular methods established in recent years, such as the polymerase chain reaction (PCR) [4-5].

The SARS-CoV-2 virus causes the New Coronavirus Disease (COVID-19), which was first described on January 13, 2020, as a result of research conducted in a group of patients in Wuhan Province, China, who developed respiratory symptoms in late December 2019 [6]. On March 11, 2020, the first COVID-19 case was discovered in our region. As of 10.01.2021, our country had recorded 2.326,256 cases and 22,807 deaths [7]. During the pandemic in our country, we tried to monitor the increase in cases by imposing curfews for children under the age of 18 and restricting their access to public spaces. For fear of sickness and pandemic limits, most parents refuse to admit their children to the hospital.

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There are a limited number of studies on viruses that cause respiratory tract infections in children. Viruses that cause respiratory infections in children in the months before the SARS-CoV2 virus appears are also a matter of curiosity. The aim of this study was to identify the causative respiratory viruses in hospitalized patients with acute respiratory tract infection in a tertiary university hospital during the fall-winter 2019-2020 season, before the COVID-19 pandemic, review clinical and laboratory results, discuss prevention strategies for the coming winter season during the ongoing pandemic process and contribute to the literature by providing data from the period just before the pandemic.

Materials and Methods

Data from patients aged one month to 18 years who were admitted to Sivas Cumhuriyet University Faculty of Medicine and hospitalized at general pediatric service and Pediatric Intensive Care Unit (PICU) due to acute upper / lower respiratory tract infections between September 1, 2019, and March 1, 2020, and who sent a respiratory virus PCR panel were retrospectively analyzed. The patients' demographics, admission month, admission symptoms, diagnoses, duration of hospital stay, PICU admissions and respiratory support treatments, clinical and laboratory findings, and multiplex PCR panel were assessed. Nasopharyngeal swab samples were tested at the Sivas Cumhuriyet University Medical Microbiology Laboratory to identify respiratory tract pathogens using the QIAstat-Dx® Respiratory Panel (Qiagen GmbH, Hilden, Germany). Twenty-one respiratory tract pathogens (adenovirus (AV), bocavirus (HBoV), coronavirus 229E (HCoV-229e), coronavirus OC43 (HCoVOC43), coronavirus NL63 (HCoVNL63), coronavirus HKU1 (HCoHKU1), rhinovirus (RV), enterovirus (EV), Human metapneumovirus A / B (hMPV), influenza A, influenza A (H1N1), influenza B, parainfluenza 1, parainfluenza 2, parainfluenza 3, parainfluenza 4, Respiratory Syncytial Virus (RSV A / B), Seasonal influenza (H1N1 / H3N2) had been studied with this panel.

Patients enrolled in the study had one or more of the following symptoms: fever, cough, rhinorrhea, headache, conjunctivitis, wheezing, and dyspnea. The medical histories and demographic details of the patients were derived from their medical records. Premature babies were described as those born before 37 weeks of gestation. The patients' diagnosis was taken from the system (3 groups as pneumonia, bronchiolitis, and upper respiratory tract infections). Chronic diseases included asthma, immunodeficiency, cystic fibrosis, neurological diseases, congenital heart disease, and etc. Patients were classified into four age ranges (<1 year old, 1-5 years old;6-10 years old; >10 years old). Leukopenia, lymphopenia, and neutropenia were defined as below 2SD for age. The study was approved by Sivas Cumhuriyet University Non-Interventional Clinical Research Ethics Committee (2020-02/35).

Statistical analysis

The analyzes were carried out with the SPSS 22. package program. Normality was checked using the Kolmogorov Smirnov test. Data were given as mean, standard deviation, median, minimum-maximum, frequency, and percentage. Normally distributed measurable data were compared in independent groups by t-test, others by Mann-Whitney U test. Categorical data were evaluated using Chi-square and Fisher's exact tests. $p < 0.05$ was considered statistically significant.

Results

The data of 139 patients admitted to the PICU or general pediatric service with the diagnosis of acute respiratory tract infection and who had a respiratory tract multiplex PCR panel were evaluated retrospectively. At least one viral pathogen was detected in 105 (75.5%) patients. 5 patients (3.59%) had co-infection. 64.4% (n = 89) of the patients were male, the median age was 23 months (min 1 max 209 months), 38.9% (n = 54) of the patients were under 1 year old. The median length of hospitalization of the patients was six days (minimum 1- maximum 26 days). The socio-demographic characteristics of the study patients are presented in Table-1.

Seventy-four patients (53.2%) were hospitalized with pneumonia, and 18 patients (13%) were diagnosed with bronchiolitis. Twenty-five patients (18%) had a history of prematurity, four patients (2.9%) had asthma, and 36 patients (25.9%) had another concomitant chronic diseases.

Table 1. Socio-demographic characteristics of the patients

Characteristics	Patients (n=139) (%)
Median age in months (minimum-maximum)	23 months (1-209)
Age group	
<1 year	54 (38.9%)
1-5 years	48 (34.5%)
6-10 years	26 (18.7%)
>10 years	11 (7.9%)
Gender	
Male	89 (64.4%)
Female	50 (35.6%)
Underlying conditions	
Prematurity	25 (18%)
Asthma	4 (2.9%)
Other cronical disesases (Cystic fibrosis, Immune-deficiency, congenital heart disease etc)	36 (25. 9%)

Overall, 110 viruses were detected. The most common detected viruses were Influenza A (H1N1) (21.8%), Influenza B (20.9%), RV (18%), and RSV (17.3%). The rate of patients without any viral pathogen was 24.4% (n = 34). Figure-1 shows the frequency of each of the viruses detected in the study population.

The most common agents in patients with pneumonia were RSV, Influenza A, Influenza B, RV (12.1% each). While the most common agent was RSV (33.3%) in hospitalized patients with bronchiolitis, Influenza A (H1N1) was the most common agent (25.5%) in patients hospitalized with upper respiratory tract infection. When the distribution of the most frequently detected viruses by age groups was examined together with co-infections, RSV (n=17, 31.4%) and RV (n=11, 18.5%) under 1 year of age, Influenza A (H1N1) (n=11, 22.9%), Influenza B (n=7, 14.5%) and Bocavirus (n=7, 14.5%) in between 1-5 years, Influenza B (n=8, 30.7%), and Influenza A (H1N1) (n=6, 23%) in between 6-10 years, and Influenza B (n=6, 54.5%) over the age of 10 were the most frequently detected viruses. The most common co-infection was RSV-RV (40%). 29.4% of the patients with RSV were premature. Premature babies was born between 30-34 weeks, and they had not received RSV prophylaxis.

A significant difference in age distribution according to viral pathogen was observed with Influenza A (H1N1) patients having a median age of presentation of 26 months (1–153) compared to 93 months (1–196) in influenza B patients, two months (1–32) in RSV patients, and 14.5 months (5–197) in RV patients ($p < 0.001$). The median age for the other detected viruses was 39 months (1-102). Patients with RSV were dramatically younger than those affected by different viruses, whereas the influenza viruses affected older children. All of the blood cultures taken from patients were negative. In addition, no substantial bacterial growth was found in throat cultures taken from patients aged five and up.

The rate of male patients (64.4%) was higher than girls. The rate of RSV, Influenza A (H1N1), Influenza B, and RV was detected higher in male patients compared to female patients, and the difference was statistically significant ($p < 0.05$).

The most common complaints of the patients were cough (87%), fever (80.6%), wheezing (55.3%), and rhinorrhea (40.3%). Fever was most common in patients with Influenza A (H1N1) and Influenza B (95.7% and 90.5%). Cough was present in all RSV, PIV 1-2-3, hMPV, and CHKU1 patients. Hypoxia was found in 52 patients (37.4%), and oxygen therapy was administered. 40.3% of the patients had tachypnea, 37.4% had retraction and dyspnea. The highest number of hospitalizations and detection of viral pathogens were in January (41.7%). Epidemiologic and clinical characteristics of children with viral acute respiratory infections are summarized in Table-2.

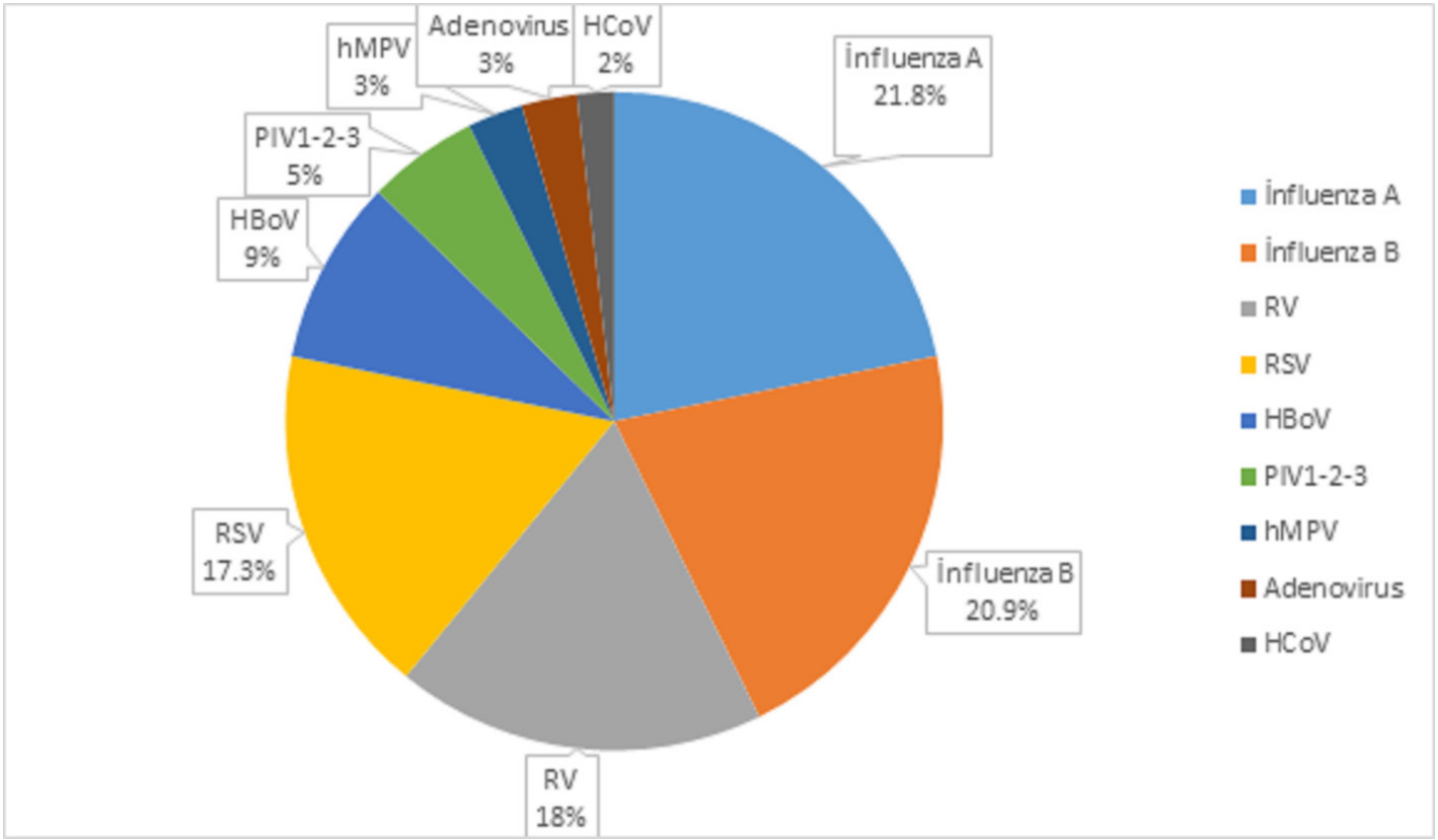

Figure 1. Distribution of the viruses with acute respiratory infections
RSV: Respiratory Syncytial Virus, RV: Rhinovirus, hMPV: Human metapneumovirus, PIV: parainfluenza virus, hBoV: human bocavirus, hCoV : human coronavirus

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Table 2. Epidemiologic and clinical characteristics of children with viral acute respiratory infection

	Any viral etiology (n=34) (%)	RSV (n=17) (%)	Influenza A (n=23) (%)	Influenza B (n=21) (%)	RV (n=16) (%)	HBoV (n=10) (%)	Adenovi-rus (n=2) (%)	hMPV (n=3) (%)	PIV 3-2-1 (n=6) (%)	HCoV (n=2) (%)	Co-inf (n=5) (%)	Total (n=139) (%)
Age												
<1 year	13 (38.2%)	15 (88.2%)	6 (26%)	1 (4.8%)	8 (50%)	2 (20%)	-	2 (66.7%)	3 (50%)	1 (50%)	3 (60%)	54 (38.9%)
1-5 years	11 (32.4%)	2 (11.8%)	11 (47.8%)	7 (33.3%)	5 (31.3%)	7 (70%)	1 (50%)	1 (33.3%)	3 (50%)	-		48 (34.5%)
6-10 years	8 (23.5%)	-	5 (21.7%)	7 (33.3%)	2 (12.5%)	1 (10%)	1 (50%)	-	-	-	2 (40%)	26 (18.7%)
>10 years	2 (5.9%)	-	1 (4.35%)	6 (28.6%)	1 (6.2%)	-	-	-	-	1 (50%)		11 (7.9%)
Gender												
Female	14 (41.2%)	6 (35.3%)	5 (21.7%)	6 (28.6%)	4 (25%)	5 (50%)	-	2 (66.7%)	4 (66.7%)	2 (100%)	2 (40%)	50 (35.6%)
Male	20 (58.8%)	11 (64.7%)	18 (78.3%)	15 (71.4%)	12 (75%)	5 (50%)	2 (100%)	1 (33.3%)	2 (33.3%)	-	3 (60%)	89 (64.4%)
Underlying Conditions												
Prematurity	7 (20.6%)	5 (29.4%)	4 (17.4%)	2 (9.5%)	3 (18.8%)	1(10%)	-	-	2 (33.3%)	-	1 (20%)	25 (18%)
Asthma	2 (5.9%)			1 (4.8%)	1 (6.2%)						-	4 (2.9%)
Other cronical disesases	9 (26.5%)	1 (5.9%)	8 (47%)	8 (38.1%)	6 (37.5%)	1(10%)	-	-	2 (33.3%)	1 (50%)	-	36 (25.9%)
Symptoms												
Fever	24 (70.6%)	12 (70.6%)	22 (95.7%)	19 (90.5%)	12 (75%)	9 (90%)	2 (100%)	2 (66.7%)	4 (66.7%)	2 (100%)	4 (80%)	112 (80.6%)
Cough	28 (82.4%)	17 (100%)	22 (95.7%)	16 (76.2%)	15 (93.8%)	8 (80%)	-	3 (100%)	6 (100%)	2 (100%)	4 (80%)	121 (87%)
Tachypnea	14 (41.2%)	10 (58.8%)	3 (13%)	3 (14.3%)	12 (75%)	5 (50%)	-	3(100%)	4 (66.7%)	-	2 (40%)	56 (40.3%)
Wheezing	21 (61.8%)	15 (88.2%)	6 (26%)	5 (23.8%)	13 (81.3%)	8 (80%)	-	3(100%)	4 (66.7%)	-	2 (40%)	77 (55.4%)
Retraction/Dispne	13 (38.2%)	9 (52.9%)	2 (8.7%)	2 (9.5%)	9 (56.3%)	5 (50%)	-	3(100%)	4 (66.7%)	-	2 (40%)	49 (35.3%)
Hypoksi	13(38.2%)	9 (52.9%)	2 (8.7%)	3 (14.3%)	11 (68.6%)	5 (50%)	-	3(100%)	4 (66.7%)	-	2 (40%)	52 (37.4%)
Rinore	14 (41.2%)	3 (17.6%)	15 (65.2%)	9 (42.9%)	3 (18.8%)	3 (30%)	2(100%)	2 (66.7%)	2(33.3%)	1 (50%)	2 (40%)	56 (40.3%)
Others (Headache, conjonktivitis, etc.)	16 (47%)	3 (17.6%)	15 (65.2%)	19 (90.5%)	7 (43.8%)	6 (60%)	2(100%)	1(33.3%)	4 (66.7%)	2 (100%)	2 (40%)	77(55.4%)
Admitted to												
PICU	14 (41.2%)	9(52.9%)	4 (17.4%)	4(19%)	9(56. %3)	5 (50%)	-	1 (33.3%)	5 (83.3%)	-	1 (20%)	52 (37.4%)
General pediatric servise	20 (58. %8)	8 (47%)	19 (82.6%)	17 (81%)	7 (43.7%)	5 (50%)	2 (%100)	2 (66.7%)	1 (16.7%)	2 (100%)	4 (80%)	87 (62.6%)
Stay length day (mean ±SD)	7.55±5.18	7.05±3.74	5.17±2.69	5.2±1.85	8±3.46	6±3.23	4.5±4.94	6.66±0.57	3.75±3.09	12.5±7.77	5±4	6.43±3.88
Diagnosis												
Bronchiloitis	4(11.8%)	6 (35.3%)	1(4.35%)	-	4(25%)	-	-	-	3(50%)	-	-	18(13%)
Pneumonia	19 (55.9%)	9 (52.9%)	11(47.8%)	10(47.6%)	9(56.3%)	8(80%)	-	3(100%)	2 (33.3%)	1 (50%)	2 (40%)	74(53.2%)
Upper respiratory infection	11(32.3%)	1 (5.9%)	11(47.8%)	11(52.4%)	3(18.7%)	2(20%)	2(100%)	-	1 (16.7%)	1 (50%)	3 (60%)	47(33.8%)

RSV: Respiratory Syncytial Virus, RV: Rhinovirus, hMPV: Human metapneumovirus, PIV: parainfluenza virus, hBoV: human bocavirus, hCoV : human coronavirus, co-inf: Co-infection

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Table 3. Laboratory findings of children with viral acute respiratory infection

	Any viral etiology (n=34)	RSV (n=17)	Influenza A (n=23)	Influenza B (n=21)	RV (n=16)	HBoV (n=10)	Adenovirus (n=2)	hMPV(n=3)	PIV 3-2-1 (n=6)	HCoV (n=2)	Co-inf (n=5)	Total (n=139)
White blood cell (/mm^3)	8310±3660	9310±4010	5780±3230	5510±3040	9500±3450	12380±3480	7210±303	11420±3825	13540±4790	11240±8651	5130±3811	8120±4234
Total lymphocyte count (/mm^3)	3450.58±2460.1	5105±2798.3	2951.3±2258	2164±1219	4669±2548.9	4048±2557	3350±551	8223±3704	5577±3021	2695±331	3227±1225	3679±2572
Absolute neutrophil count (/mm^3)	4055±3356	3195±2564	2553±2016	2672.± 1821	4741±2717	7140±4157	3060±1088	2323±1840	6597±3774	8270±886	2345±1539	3854±3249
Hemoglobin (g/dl)	11.9±1.7	11.6±1.54	11.8±1.67	13±1.34	11.6±1.01	11.3±1.61	13±0.42	10.4±0.4	12.3±2.7	10.3±3.8	12.3±1.01	11.9±1.64
Platelet (/mm^3)	326±153	409±89.7	221±108	190±70	389±171	417±143	305±54	191±50	400±151	430±184	331±194	313±154
CRP*(mg/dl) (median-min/max)	4.25 (1.15-87)	6.73 (1-18.5)	8.2 (1.02-154)	3.89 (1-55)	6.74 (1.21-59.9)	18 (2.38-58)	8.72 (3.24-14.2)	1.72 (1.28-15)	8.6 (4.58-31)	62.5 (61-63)	4.1 (1.72-7.22)	5.54 (1-154)

Data was given as mean ±SD *CRP was given as median-min/max
RSV: Respiratory Syncytial Virus, RV: Rhinovirus, hMPV: Human metapneumovirus, PIV: parainfluenza virus, hBoV: human bocavirus, hCoV : human coronavirus, co-inf: Co-infection

Fifty-two patients (37.4%) were followed up in PICU, and 87 patients (62.6%) in the general pediatric service. The 3 most common viral pathogens isolated in PICU were RSV (17.3%), RV (17.3%), and HBoV (9.6%). 42.5% (n = 17) of those with chronic disease, and 72% (n = 18) of those with a history of prematurity needed intensive care and were followed up in PICU. Oxygen therapy with a high flow oxygen device (HFNC) was given to 35 patients (25.1%) in total. 50% of the patients with HBoV and 43.75% of the patients with RV had received HFNC treatment. Thirty-three patients were given systemic steroids (23.7%). All patients admitted to the PICU received antibacterial therapy. All Influenza positive patients in the PICU and general pediatric service received oseltamivir medication; no other antiviral treatment was provided to any patients.

The mean white blood cell count (WBC) of the patients with at least one respiratory tract virus was 8120 ± 4235/mm^3, the mean total lymphocyte count was 3679 ± 2572, and the median value of C-reactive protein (CRP) was 5.54 mg/dl (minimum one and maximum 154 mg/dl). Leukopenia was found in 26 (24.8%) of the patients, neutropenia in 32 (30.5%), and lymphopenia in 37 patients (35.2%). Patients with influenza A (H1N1) had neutropenia in 37.5% and lymphopenia in 33.3%, while patients with influenza B had lymphopenia in 39.1% and neutropenia in 43.4%. There was no statistically significant difference when laboratory values were analyzed by separating the patients with at least one respiratory tract virus into six groups: RSV, Influenza A (H1N1), Influenza B, RV, HBoV, and other viruses ($p > 0.05$). Leukocyte and lymphocyte counts of influenza cases were lower than the other groups, but the difference was not statistically significant ($p > 0.05$). Laboratory findings of children with viral acute respiratory infections are given in Table-3.

Discussion

Respiratory viruses are the most common cause of respiratory tract infections in children. They can cause a wide range of clinical symptoms, from a simple upper respiratory infection to multiple organ failure and death [1]. Acute lower RTIs are estimated to kill 1.3 million children under five years worldwide per year [8]. Children under the age of five are particularly vulnerable in developing and underdeveloped countries. In this study, we examined respiratory tract viruses in hospitalized children diagnosed with RTIs between September 2019 and March 2020. At least one viral respiratory tract pathogen was detected by molecular method (multiplex PCR) in 75.5% of our cases. In similar studies from our country, this rate ranges from 36.3% to 78.6% [9-12]. Since we evaluated only inpatients in our study, the rate of virus detection may be higher for this reason. Also, it should be taken into account that the survey covered the season in which respiratory tract infections were most common and the multiplex PCR kit used to detect 21 respiratory tract pathogens.

The distribution and frequency of respiratory viruses vary, depending on factors such as age, socioeconomic level, underlying disease, season, and the scope of the PCR test applied. The dominant viruses in this study were influenza A (H1N1), influenza B, and RV. Avcu et al. found that 28.7% RSV and 22.3% RV in children aged 0-18 were hospitalized due to lower respiratory tract infections [13]. Karadag-Oncel et al. found 39.2% influenza A (H3N2), 23.5% influenza B, 15.6% RSV in children in the same age range presenting with influenza-like symptoms [10]. Akturk et al. found influenza A (H3N2) was 16.4%, RSV 9.2% in 33.5% of patients over two years of age with respiratory tract infections [9]. In a study involving both children and adults, influenza A (H1N1) was found to be present at a rate of 12.1%, RSV at 11.0%, and RV at 5.6% [12]. RSV is a significant cause of lower respiratory tract diseases, especially in young children. In studies involving younger patients, the detection rate of RSV ranges from 35-61.2% [14-17]. In our study, following the literature, RSV was the most common viral agent under the age of one, with a rate of 31.4%. When all age groups were combined, influenza A (H1N1) and influenza B were the most common viruses. Consistent with the literature, influenza patients were older (influenza A median 26 months, influenza B median 93 months). Other respiratory viruses' frequency is thought to vary depending on the severity of seasonal influenza epidemics, but the distribution pattern remains consistent in general [9]. Our study was conducted during the influenza season, so it is expected that influenza A (H1N1) and influenza B viruses were the most common agents. January and March are the periods when viral infections peak. In studies conducted in our country, December was considered the month with the most viral infections [18]. In our study, the highest number of hospital admissions and detection of viral pathogens was in January.

New viruses such as HMPV, HBoV, and multiple viral infections have begun to be detected while the introduction of PCR kits working with the multiplex method. The rate of multiple infections varies in publications from all over our country (2.8-30.9%), and the rate of multiple infections found in our study is similar to our regions data (3.59%) [9,11,13,19-21]. In our study, RSV-RV association was the most common multiple infections (40%), as in other similar studies conducted in our country [19-21].

Age is always an essential factor in predicting the causative microorganism in childhood infections. It is also important to know the age distribution of respiratory tract viruses. When our cases are divided according to age groups, it is noteworthy that the most common causative agent viruses are different. In our study, 38.4% of the patients were under one year of age, and RSV was the most common viral agent under the age of one with a rate of 31.4%. Approximately one-third of the patients with RSV were premature. Karakoyun et al. found that the frequency of RSV infection was 63% in their study, they evaluated hospitalized babies at 0-24 months of age due to respiratory tract infection, and the prematurity rate was higher than patients without RSV [22].

In our study, RSV was the most frequently detected viral pathogen in patients hospitalized with a diagnosis of bronchiolitis and pneumonia. Mengelle et al. found that RV (40%) was the most prevalent pathogen in upper respiratory tract infections, and RSV (49.9%) was the most prevalent in lower respiratory tract infections [17].

In our study, neutropenia was found in 37.5% of patients with influenza A (H1N1), leukopenia 33.3%, lymphopenia was found in 39.1% of patients with influenza B, and neutropenia in 43.4%. Similar rates of leukopenia, lymphopenia and neutropenia were found in a small number of studies examining the hematological effects of influenza viruses [9,23].

In our study, 37.4% of the patients were followed up in the

pediatric intensive care unit. In a national survey of pediatric patients hospitalized in the PICU with a viral respiratory tract infection diagnosis, the most common viral agents were RSV 45%, RV 27.9%, and PIV 7.5%. 57.5% of the patients had received high flow oxygen therapy [18]. In international studies involving viral respiratory tract pathogens in pediatric intensive care units, RSV and RV are seen as the most common agents [24,25]. In our study, RSV (17.3%), RV (17.3%), and HBoV (9.6%) were the most frequently isolated viruses in patients hospitalized in the PICU, and our findings were consistent with the literature. 50% of the patients with HBoV and 43.75% of the patients with RV had received HFNC treatment. We interpreted this result as HBoV and RV infections were more severe than other viral pathogens and caused more respiratory distress. There were many examples of critically ill children with HBoV infection in the literature [26].

The most common complaints of the patients in our study were cough (87%), fever (80.6%), wheezing (55.3%), and rhinorrhea (40.3%). Unuvar et al. found that, cough and rhinorrhea were the most common complaints (91.6% -86.6%) [27]. Sik et al. found in their study in which they evaluated viral respiratory tract pathogens in patients hospitalized in the PICU, cough (40%), wheezing (37.5%), rhinorrhea (26.3%), fever (17.5%), and cyanosis (7.5%) were the most common complaints [18]. The rate of respiratory symptoms like cough and wheezing was comparable to the literature in our research, but the rate of fever was higher [10,20,21]. Patients with influenza A (H1N1) and influenza B had particularly high fever. According to the literature, the involvement of patients hospitalized with a diagnosis of upper respiratory tract infections was the explanation for the higher incidence of fever.

In our study, the number of male patients was higher, while RSV, influenza A (H1N1), influenza B, and RV were significantly higher in male patients. In some studies in the literature, viral agents were found to be slightly higher in male patients [21,27,28]. This difference in our study was interpreted as that male patients were brought to hospitals more often by their families, and hospitalization rate was higher. We also determined that influenza and other respiratory tract viruses cause diseases with similar symptoms; although leukopenia/lymphopenia is more common in influenza cases, it has been concluded that we cannot make a definite distinction clinically and laboratory.

In this study, most of the children (75.5%) who were admitted to a tertiary university hospital with a diagnosis of respiratory tract infection, had at least one respiratory tract virus, and gave information about the age, and month distribution of viral infections. It was observed that RSV infections caused hospital admissions, especially in patients under one year of age. While RSV-related mortality rate is reported as 0.5-1% in previously healthy babies, this rate rises to 3-5% in premature babies with chronic lung disease, and up to 33% in those with severe heart diseases [29]. Families do not want to admit to the hospitals during the pandemic process, but the RSV prophylaxis of premature babies should be continued as soon as possible. In our study, influenza A H1N1 was observed in all influenza cases, influenza A H3N2 was not detected. 74% of the patients with influenza A (H1N1) were older one year. The fact that influenza is the most common factor among all viral agents, emphasizes the importance of influenza vaccines. During the COVID-19 pandemic, the World Health Organization (WHO) recommends that all children between the ages of 6 months and 5 years, and children with chronic diseases of all age groups should have influenza vaccination at the beginning of the influenza season [30]. Immediate vaccination is important to keep them safer during the pandemic process.

Identifying the causes is critical both epidemiologically and clinically. It allows us to generate valuable data ranging from the location and distribution of the agent to individual isolation, and a deeper understanding of the disease. Rapid and sensitive diagnosis of viruses that cause respiratory tract infections is important in preventing unnecessary antibiotic use, developing antibiotic resistance, and reducing morbidity.

With this study, respiratory viruses that caused hospitalization in different pediatric age groups during the influenza season before the COVID-19 pandemic were detected, the patients were evaluated with clinical and laboratory findings. This data will contribute to the literature for both our province and our country. We also shared protection recommendations.

Study limitations

Since the study was conducted retrospectively, the patients' data were obtained from patient files and hospital automation systems. There might have been deficiencies, and errors in some data. The physical examination findings of the patients were not included in the study due to data deficiencies. The diagnoses are taken as they are recorded in the patient files retrospectively; there may be diagnostic flaws and errors, especially in the distinction between viral pneumonia and bronchiolitis. Another limitation of the study was bacterial coinfections. Although there were no positive blood and throat cultures, we could not completely ruled out accompanying bacterial infections. The indications for PICU admissions could not be clearly stated while the same reasons. There was no information on RSV prophylaxis in infants with congenital heart disease. Prospective studies involving more patients and covering the whole year will be much more guiding.

Conclusion

We observed that different agent viruses in different age groups cause respiratory tract infections in children. Unnecessary antibiotic use and morbidity can be reduced by detecting the viral agent in the early period with the PCR method. It is essential to continue prophylaxis with a monoclonal antibody against RSV without interruption at risk group patients, and vaccination against influenza during the COVID-19 pandemic process. It should be kept in mind that respiratory tract infections may progress slowly and cause mortality/morbidity, especially in children with prematurity and underlying diseases.

Conflict of interests
The authors declare that they have no competing interests.

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Ethical approval
Sivas Cumhuriyet University Non-Interventional Clinical Research Ethics Committee (2020-02/35)

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