Original Investigation / *Özgün Araştırma*

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Distribution and Clinical Features of Viral Respiratory Infections in Children After Face-To-Face Education in 2021-2022 Winter Period

2021-2022 Dönemi Yüz Yüze Eğitime Tam Geçiş Sonrası Çocuklarda Görülen Viral Solunum Yolu Virüslerinin Dağılımı ve Klinik Özellikleri

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Abstract

Objective: Several public health measures were introduced to reduce viral transmission and disease spread at the beginning of the COVID-19 pandemic. These measures had the potential to impact the transmission of other respiratory viruses. In September 2021, schools started face to face in and an increase in viral respiratory infections was observed. This study aims to determine the distribution and clinical features of viral agents in this period when complete face-to-face education was started for the first time in Turkey.

Material and Methods: Diagnosis and clinical data of the pediatric patients who were tested for respiratory viral infections between October 1, 2021-January 1, 2022 were retrospectively retrieved from hospital records. Viral agents detected by polymerase chain reaction (PCR) in the nasopharyngeal aspirate samples obtained at the first application of the patients during the pandemic period were investigated.

Results: There were 404 patients who were diagnosed with respiratory tract infections and tested for respiratory viruses. The leading viral agents in children who applied to our center between October and December 2021 were COVID-19 (32.7%), multiple viral agents (23.9%), RSV (15.3%) and rhinovirus (8.7%). 43.8% of patients diagnosed with RSV needed hospitalization.

Conclusion: Our study shows that after complete face-to-face education and, the viral diversity is observed again in this winter period like before the pandemic. The high rate of hospitalization in RSV cases was remarkable.

Keywords: Respiratory viral infections, pandemic, pediatric, face-to-face education

Öz

Giriş: COVID-19 pandemisinin başlangıcında viral bulaşmayı ve hastalık yayılmasını azaltmak için çeşitli halk sağlığı önlemleri uygulamaya konuldu. Bu önlemler, diğer solunum yolu virüslerinin bulaşmasını da etkileme potansiyeline sahipti. Eylül 2021'de okullarda tamamen yüz yüze eğitime geçildi ve viral solunum yolu enfeksiyonlarında artış gözlemlendi. Bu çalışma, Türkiye'de ilk kez tam yüz yüze eğitimin başladığı bu dönemde viral etkenlerin dağılımını ve klinik özelliklerini belirlemeyi amaçlamaktadır.

Gereç ve Yöntemler: 1 Ekim 2021-1 Ocak 2022 tarihleri arasında solunum yolu multipleks PCR testi yapılan çocuk hastaların tanı ve klinik verileri hastane kayıtlarından geriye dönük olarak alındı. Pandemi döneminde hastaların ilk uygulamasında alınan nazofaringeal aspirat örneklerinde polimeraz zincir reaksiyonu (PCR) ile saptanan viral ajanlar araştırıldı.

Bulgular: Solunum yolu enfeksiyonu teşhisi koyulan 404 hasta vardı. Ekim-Aralık 2021 tarihleri arasında merkezimize başvuran çocuklarda önde gelen viral ajanlar COVID-19 (%32.7), çoklu viral ajan (%23.9), RSV (%15.3) ve rinovirüs (%8.7) olmuştur. RSV tanısı konan hastaların %48.3'ünün hastaneye yatırılması gerekmiştir.

Sonuç: Çalışmamız, yüz yüze eğitime tamamen geçildikten sonra, pandemi öncesinde olduğu gibi kış dönemindeki viral çeşitliliğin yeniden gözlemlendiğini göstermiştir. RSV vakalarında hastaneye yatış oranının yüksek olması dikkat çekten önemli bir bulgudur.

Anahtar Kelimeler: Solunum yolu virüsleri, pandemi, pediyatri, yüzyüze eğitim

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Introduction

A novel coronavirus was identified which caused a cluster of pneumonia cases in Wuhan, a city in the Hubei province of China at the end of 2019. It rapidly spread, and resulted in an epidemic throughout China, followed by an increasing number of cases globally. In February 2020, the World Health Organization (WHO) designated the disease COVID-19 (coronavirus disease 2019) and declared it as a pandemic (1). Children of all ages can get COVID-19 (2). The incidence in children is similar to that in adults but they generally have a lower risk of exposure and are tested less frequently than adults (3). Besides they are known to have milder diasese than adults. In surveillance from various countries children typically account for up to 18 percent of laboratory-confirmed cases (4).

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) mainly transmits through respiratory droplets as other coronaviruses. Aerosol transmission may occur in specific settings, mainly indoor, crowded, and inadequately ventilated spaces (5).

Several public health measures were applied to control the pandemic which varied between countries. These interventions included physical distancing, stay-at-home orders, school closures, travel restrictions, and border closures (6). These measures had the potential to impact transmission of other respiratory viruses; therefore 98.0% and 99.4% reductions of respiratory syncytial virus (RSV) and influenza virus detections were reported, respectively (7,8). Besides, seasonal delay shift was observed in RSV infection (8).

Similarly, in our country, in the 2020-2021 academic year, the winter semester was completed mainly with online education in line with the Ministry of National Education and Ministry of Health. Due to these restrictions, infections due to RSV, influenza were decreased in the 2020-2021 winter term (9).

In September 2021schools started face to face in accordance with the academic calendar, and an increase in viral respiratory infections was observed.

The aim of this study was to determine the distribution and clinical features of viral agents in this period when complete face-to-face education is started for the first time in Turkey and to observe whether there was a seasonal shift related to viruses.

Materials and Methods

This retrospective study was conducted in Gazi University, Pediatric Infectious Diseases Department. Patients who applied with respiratory tract symptoms and underwent respiratory multiplex PCR (polymerase chain reaction) were included in the study. Age, gender, diagnosis, need for hospitalization were retrieved from computerized hospital records. The number of outpatients and inpatients who were admitted to our hospital respiratory tract infection (including COVID-19) monthly from October 1, 2021 till January 1 January 2022 were analyzed.

In this study, we evaluated a multiplex real-time PCR panel for the simultaneous detection of 21 types of respiratory viral pathogens (Influenza A, Influenza B, H1N1, human parainfluenza (PIV 1, PIV 2, PIV 3, PIV 4), human rhinovirus, human coronavirus (NL63-229E-OC43-HKU1), human metapneumovirus A/B, human bocavirus, human respiratory syncytial virus A/B, human adenovirus, human parechovirus, enterovirus) using Fast Tract Respiratory Pathogens 21 (Siemens Healthcareb GmbH, Germany) in nasopharyngeal specimens of the patients with respiratory tract infections.

All data was entered into the SPSS program. Statistical analyses were carried out using IBM SPSS Statistics, version 22 (SPSS Inc, Chicago, IL, USA). Descriptive statistics were used to calculate frequency and percentage distributions. Median, minimum and maximum were used for continuous variables that didn't distribute normally.

Comparison of categoric variables was performed using the chi-square test. Continious variables were compared with Mann Whitney u test.

The study was conformed with the principles of the Declaration of Helsinki and was approved by the local ethics committee and the Institutional Review Board of Gazi University Clinical Research in 2022/January.

Results

There were 404 patients who were diagnosed with respiratory tract infections and were tested for respiratory viruses. The median age of these patients was 56.4 months (18 days- 17.9 years). 56.9% (n= 230) of the patients were male and 43.1% (n= 174) were female. 23.5% (n= 95) of the patients needed hospitalization and 76.5% (n= 309) were followed as outpatients. 73.5% (n= 297) of the patients was diagnosed with upper respiratory infection, whereas 26.5% (n= 107) was diagnosed with viral pneumonia, %18.1 (n= 73) of patients who were diagnosed with upper respiratory infection had fever for 72 hours or longer. 28.5% (n= 115) of patients were followed in October, 35.9% (n= 145) of patients were followed in November and 35.6% (n= 144) were followed in December 2021. The data of the patients are shown in Table.

The respiratory viral multiplex PCR results of patients were as follows: 32.7% (n= 132) of patients were positive for COVID-19, 15.3% (n= 62) were positive for human respiratory syncytial viruses A/B (RSV), 8.7% (n= 35) were positive for rhinovirus, 6.4% (n= 26) were positive for influenza virus, 3.2% (n= 13) were positive for coronaviruses (HCoV), 3.2% (n= 13) were positive for bocavirus, 2.7% (n= 11) were positive for human parainfluenza virus, 2.2% (n= 9) were positive human-metap-

neumovirus and 1.5% (n= 6) were positive for human adenovirus. Ninety-seven patients were positive for multiple viruses at the same time. When comparing COVID-19 with other respiratory viruses, hospitalization was significantly lower in patients infected with viruses other than COVID-19 (p= 0.000).

When we excluded patients with COVID-19, there were 272 patients totally. Median age was 42 months of age (18 days-17.9 years). The age of hospitalized patients was significantly younger than patients who were not (p= 0.003). There were 157 boys (57.7%) and 115 girls (42.3%). There was no significant difference between genders in case of hospitalization (p= 0.112). The final diagnosis of 165 patients was URI (59.6%) and 107 (42.3%) was LRI (p= 0.000). The distribution of viruses in multiplex PCR is shown in Table 1. There was no statistically significant difference between different viruses in case of hospitalization (p= 0.09).

The monthly distribution of respiratory viruses is shown in Figure 1. When COVID-19 was excluded, multiple virus positivity on multiplex PCR was most commonly observed in all three months (31.7% in October, 39.7% in November and 33.0% in December). Respiratory sincytial virus (29.3%) was the second most common cause of respiratory tract infections with rhinovirus (13.8%) in November and RSV (22.6%) and influenza virus (21.7%) were the most commonly isolated causes of respiratory tract infections in December 2021.

Discussion

To the best of our knowledge, this is the first pediatric study on the distribution of respiratory tract viruses in children after the complete transition to face-to-face education during the pandemic process in Turkey.

In Turkey, schools opened in September 2021 and face-to-face education literally started over. Using face masks and physical distance practices continued in schools with the advice of the Ministry of Health and Ministry of Education (9).

Table 1. The distribution of respiratory viruses on multiplex PCR of patients

	Total	Outpatient	Inpatient	p
Age median (min-max)	42 months (18 days-17.9 years)	46.8 months (24 days-17.9 years)	26.4 months (18 days-17.9 years)	0.003
Gender				
Male	157 (57.7%)	96 (54.2%)	61 (64.3%)	0.112
Female	115 (42.3%)	81(45.8%)	34 (35.7%)	
Diagnosis				
URI	165 (59.6%)	132 (74.6%)	33 (34.7%)	0.000
LRI	107 (39.3%)	45 (25.4%)	62 (65.3%)	
Viral multiplex PCR				
HCoV	13 (4.8%)	7 (4%)	6 (6.3%)	0.09*
Influenza virus	26 (9.6%)	20 (11.3%)	6 (6.3%)	
RSV	62 (22.8%)	32 (18.1%)	30 (31.6%)	
Rhinovirus	35 (12.9%)	23 (13%)	12 (12.6)	
HMPV	9 (3.3%)	6 (3.4%)	3 (3.2%)	
Parainfluenza virus	11 (4.0%)	8 (4.5%)	3 (3.2%)	
Bocavirus	13 (4.8%)	7 (4%)	6 (6.3%)	
Adenovirus	6 (2.2%)	4 (2.3%)	2 (2.1%)	
Multiple viruses	97 (35.7%)	70 (39.5%)	27 (28.4%)	

*p value is for comparison of viruses with each other in case of hospitalization.

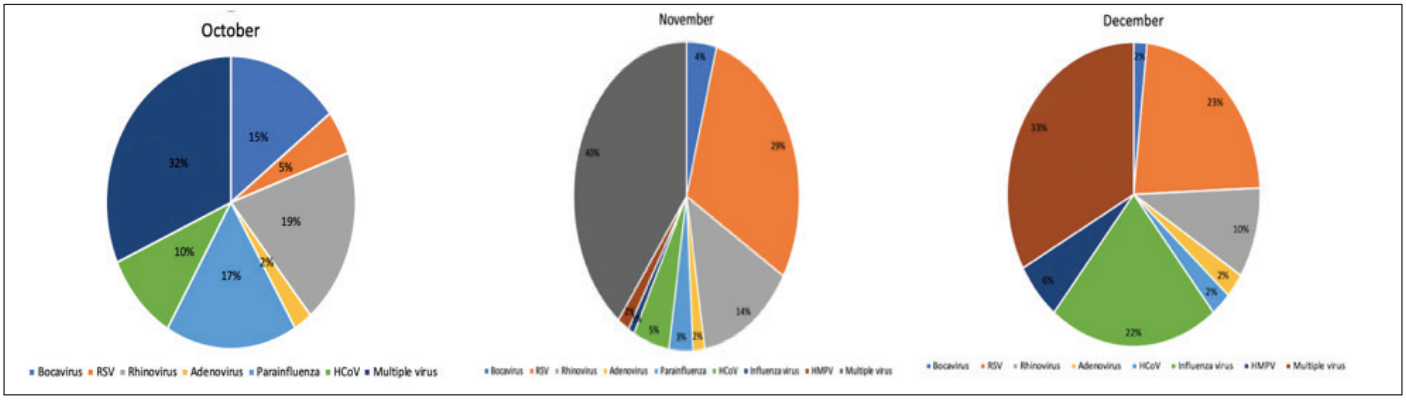

Figure 1. Monthly distribution of respiratory viruses (COVID-19 excluded).

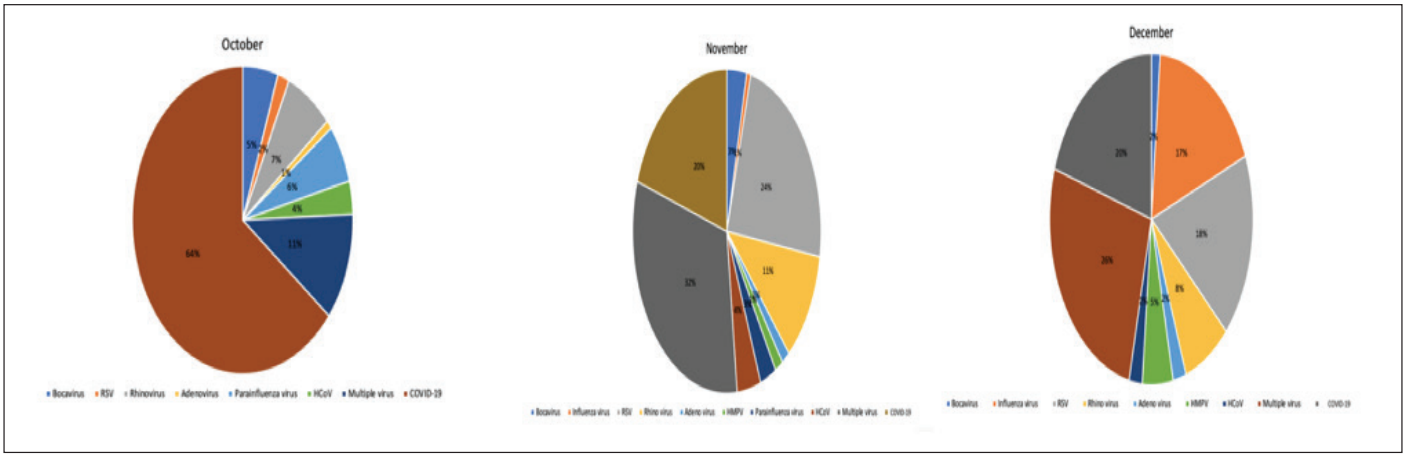

Figure 2. Monthly distribution of respiratory viruses (COVID-19 excluded).

Turkey is located in the North hemisphere and this means, RSV and influenza are common causes of respiratory infections in winter season. Influenza activity in the North hemisphere can occur anytime from October to May but most commonly peaks between December and February. Seasonal epidemics can last 8 to 12 weeks or longer (10). Similarly, RSV occurs in annual epidemics generally beginning in fall and continuing through early spring in temperate climates (11). After measures like physical distancing, stay-at-home orders, school closures and travel restrictions in the 2020-2021 winter during the COVID-19 pandemic, the impact of COVID-19 measures on the spread of other viral diseases was observed strikingly and clearly in our country (9). Similar reports supported this reduction from all over the World. Yoeh et al. observed a similar initial reduction in RSV and influenza detections among Australian children followed by a near-complete absence over the subsequent four months, confirming that low RSV and influenza activity has been sustained in Western Australia throughout the winter period (7).

After these developments, reports showing an unprecedented reduction of RSV, ADV, FluA, FluB, and MPV infections during the pandemic, despite the reopening of schools increasingly appeared (12). Besides, Agha et al. reported a seasonal shift and delayed peak of RSV in young children after reopening of schools. First RSV cases were seen in February 2021, and a peak was observed in April according to her study (8). In this study, it was observed that influenza and RSV cases began to increase in the expected season. So the delay was not observed differently from the literature.

According to our study, the most common result of multiplex PCR was the detection of many viruses (viral co-infection) at the same time. It is a known fact that the viral shedding of many respiratory tract viruses, including COVID-19 continues after infection. According to a report, this prolonged viral shedding may be observed with 60% of especially immune-compromised individuals excreting viruses for >10 days (13). This period is reported as high as several weeks in COVID-19 (14). The result of the simultaneous detection of many viruses in our study may be because, children are exposed to many respiratory viruses one after another in the winter season. So, after especially relaxation of control measures and reopening of schools, despite the pandemic, viral diversity was observed like earlier years. Moreover, when the winter months began (after October), other viruses began to overtake COVID-19 in total.

The data by Agha et al. indicated more severe disease with RSV in younger infants and this fact was attributed to possible deficient immunity from a lack of exposure to RSV in the previous season (8). The median age of the cohort was six months (12 days to 9 years). 66.7% of patients were hospitalized, and 81% of them were admitted to the intensive care unit. This condition was attributed to possible deficient immunity. According to our data, RSV was the second most common viral agent observed in % 22.8 of patients (when COVID-19 is excluded). An interesting finding was that almost half of the (48.3%) patients diagnosed with RSV needed hospitalization in this period. Large-scale and well-designed prospective studies are warranted to support this critical finding.

A study by Liu et al. showed a sharp increase in rhinovirus infection after the reopening of schools (12). A similar rise in rhinovirus infection was observed by Yigit et al. (9). In our study, rhinovirus was 12.9% (COVID-19 excluded) of total patients and this striking rise was not observed.

Although clinical features of COVID-19 is not the purpose of this study, the results of this study supported the fact that COVID-19 has a milder course in children. This study was completed just before the increase in cases due to omicron and delta being the dominant strain. The hospitalisation was significantly lower in COVID-19 cases than other viruses.

Limitations of this study are the lack of detailed laboratory data, clinical findings and confounding factors such as underlying diseases were not specified. It would be appropriate to support this data with future well-designed studies.

In conclusion, this report is important because it includes the newest data after complete face-to-face education and shows the viral diversity in this winter period. The most common viral agents in children who applied to our center between October and December 2021 were COVID-19, viral co-infections, RSV and rhinovirus. Influenza and RSV showed expected peak for their seasonality. The high rate of hospitalization in RSV cases was remarkable and must be supported in detail with future studies.

Ethics Committe Approval: The ethical approval for this study was obtained from Gazi University Clinical Research Ethics Committee (Date: 24.01.2022, Decision No: 57).

Informed Consent: Patient consent was obtained.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept- TBD; Design- TBD; Supervision- AT, HT; Resource- AT; Data Collection and/or Processing- NAÜ, NK; Analysis and/or Interpretation- TBD, NAÜ; Literature Search - TBD, EG, Writing- TBD, NAÜ, GB; Critical Review- TBD, AT.

Conflict of Interest: All authors declare that they have no conflicts of interest or funding to disclose.

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