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Investigation of the epidemiological characteristics of rhinovirus infections in patients admitted to our hospital

Ayfer Bakır[1*], Nuran Karabulut[2], Sema Alacam[3], Sevim Mese[4], Ali Agacfidan[5]
[1-5] Department of Medical Microbiology, Division of Virology and Fundamental Immunology, Istanbul University, Istanbul Faculty of Medicine, Istanbul, Turkey

Abstract
Rhinovirus (RV) is the most common cause of upper respiratory tract infections worldwide. RV can cause fatal pneumonia especially in infants, children, the elderly and immunocompromised patients. In this study, we aimed to evaluate RV distribution, comorbid mixed infection agents, age and seasonal relationships in children and adults retrospectively.
In this study, between April 2015 and March 2018, in the nasopharyngeal swab samples taken from patients with suspected respiratory tract infection, RV and other respiratory viruses were investigated by multiplex real time PCR method.
Of the 3833 patients with respiratory tract infection, 28.7% (1100) were adults and 71.3% (2733) were pediatric patients. RV was found in 15.2% of the patients included in the study. RV was defined as 18.6% (507/2733) in children and 6.8% (75/1100) in the adult age group (p <0.001). Mixed infection was detected in 33.5% (195/582) of the patients with RV. Respiratory syncytial virus (RSV) was the most frequently detected infection in children and adults (p: 0.96). According to age groups, the highest rate of RV was detected in <1 year olds. The most positive rates were found in spring and autumn.
RV was found to be higher in children than in adults and was mostly detected in children under five years of age. The most common mixed infection was RSV. In addition to its epidemiological importance, determination of RV rates and its association with high rates of RSV is of great importance especially for the follow-up and treatment planning and epidemiology of children under five years of age.

Keywords: rhinovirus, respiratory syncytial virus, respiratory tract infection

1. Introduction
Human rhinovirus (HRV), first described in 1950, is a small, positive polarity, single-stranded RNA virus classified in the Enterovirus genus of the Picornaviridae family [1]. Three different types of HRV-A, B, C have been identified and show high genetic diversity with more than 100 serotypes. HRV-A and B have been known since 1950. HRV-C was defined by molecular methods in 2006 [2]. HRVs are transmitted by direct contact, by aerosol or by means of fomites [3]. HRVs, a non-enveloped virus, are resistant to alcohol hand disinfectants and can be detected on environmental surfaces for a long time [4]. HRV is frequently responsible for the common cold, acute otitis media, rhinosinusitis and croup etiology [4, 5]. It is responsible for more than 50% of the aetiology of colds [6]. In 20% of healthy individuals, asymptomatic HRV infections are seen, whereas in symptomatic individuals it is 8-50% [7]. HRV plays an important role in lower respiratory tract infections, including pneumonia, asthma and bronchiolitis in children, the elderly and immunocompromised individuals [1, 8]. HRV is reported to be responsible for 2-17% of community-acquired pneumonia and 26% of pneumonia in children [9]. There is evidence that HRV-C may be more associated with lower respiratory tract infections than HRV-A and HRV-B [4, 10].
As with other viruses, the epidemiology of HRV differs according to geographical regions [1]. HRV infection occurs most often in the beginning of autumn and in spring [4, 11]. Revers-Transcription PCR (RT-PCR) is the most commonly used method in the diagnosis of HRV. RT-PCR is a more sensitive diagnostic method than cell culture. The distinction of HRV-A and B is done with serotype specific antisera. The most recently identified HRV-C genogrup can be detected by molecular methods and cannot be used in the definition of conventional serotyping [12]. Revers-transcription PCR (RT-PCR) is the most commonly used method in the diagnosis of HRV. RT-PCR is a more sensitive diagnostic method than cell culture. The distinction of HRV-A and B is done with serotype specific antisera. The most recently identified HRV-C genogrup can be detected by molecular methods and traditional serotyping cannot be used for identification [12].
In this study, RV and other accompanying respiratory viruses were examined by multiplex real time PCR method in nasopharyngeal swab samples taken from patients with suspected respiratory tract infection. In addition, age, gender and seasonal distribution of HV patients were determined.

2. Materials and methods
In this study, between April 2015 and March 2018, 3833 nasopharyngeal swab samples from patients with respiratory tract infection sent to Istanbul University, Faculty of Medicine,

Department of Medical Microbiology, Virology and Fundamental Immunology Laboratory were investigated by multiplex real time PCR method.

In all samples, using the FTD Respiratory pathogens 21 (Fast-Track Diagnostics, Luxembourg) kit, RV and other viruses involved in the respiratory panel (Adenovirus, Bocavirus, Coronavirus 229E, Coronavirus HKU1, Coronavirus NL63, Coronavirus OC43, Enterovirus, Human metapneumovirus A / B, Influenza A, Influenza A (H1N1), Influenza B, Parainfluenza 1-4, Parechovirus, Respiratory syncytial virus A / B) were investigated. The samples of nasopharyngeal swabs that were sent to the Microbiology Laboratory within the appropriate transport conditions and duration were kept at + 4ıC until the test run time. Viral genome extraction was obtained using Qiagen EZ1 Virus Mini Kit v2.0 (Qiagen, Germany). The product obtained after extraction was subjected to amplification on Rotor Gene Q Real-Time PCR Device (Qiagen, Hilden, Germany). This study was carried out with the approval of Istanbul University Non-Interventional Clinical Research Ethics Committee (reference no: 2018/613/08).

Statistical analysis

SPSS25 (SPSS Inc, Chicago, IL, USA) package program was used for statistical evaluation of the data. Continuous data were given as mean and standard deviation, and categorical data were given as number and percentage. Visual properties (histogram and probability graphs) and Kolmogorov-Smirnov test were used for normal distribution of variables. Student's T test or Mann-Whitney U test were used to compare the variables. Qualitative variables were compared using Pearson Chi-Square or Fisher exact tests. A p value of <0.05 was taken as the statistical significance level.

3. Results

of the 3833 patients with respiratory tract infections, the median age was 4 (range 0-100), 28.7% (1100) were adult and 71.3% (2733) were pediatric patients. RV was detected in 15.2% (582/3833) of the patients included in the study. RV was defined as 18.6% (507/2733) in the pediatric group and 6.8% (75/1100) in the adult age group (p <0.001) (Figure 1).

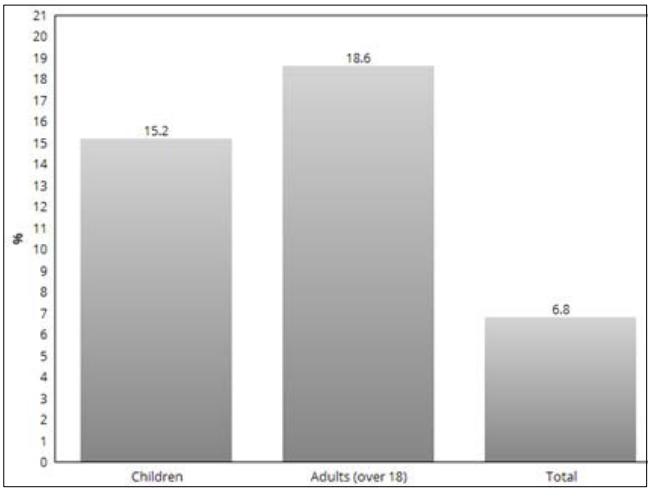

Fig 1: Rates of rhinovirus positivity in children, adults and all age groups

The median age of the patients with RV was 1 (age range, 0-92), and the rate of RV positivity was 15.5% (328/2113) for male patients and 14.8% for female (254/1720) (male/female ratio; 1.29/1) (p: 0.52). Mixed infection was detected in 33.5% (195/582) of the patients with RV. The most common cause of mixed infection was Respiratory syncytial virus (RSV) in both child and adult age group (p: 0.96) (Table 1).

Table 1: Demographic characteristics and laboratory findings of patients

		Total N (%)	**Children N (%)**	**Adult N (%)**	***p* value**
Gender	Female	1720 (44.9)	1158 (42.4)	562 (51.1)	<0.001
	Male	2113 (55.1)	1575 (57.6)	538 (48.9)	
Age (median)		4	1.0	50	
Mono infection		387 (66.5)	334	53	0.41
Mixed infection		195 (33.5)	173	22	
	RSV	63 (10.8)	55 (9.4)	8 (1.4)	0.96
	Coronaviruses*	31 (5.3)	28 (4.8)	3 (0.5)	0.64
	Adenovirus	26 (4.5)	23 (4.0)	3 (0.5)	1.00
	Bocavirus	26 (4.5)	24 (4.1)	2 (0.4)	0.56
	PIV-1,2,3,4	16 (2.7)	13 (2.2)	3 (0.5)	0.61
	Inf A	16 (2.7)	13 (2.2)	3 (0.5)	0.45
	HMPV	15 (2.6)	14 (2.4)	1 (0.2)	0.71
	Inf H1N1	11 (1.9)	11 (1.9)	0	0.38
	Inf B	11 (1.9)	10 (1.7)	1 (0.2)	1.00
	EV	7 (1.2)	6 (1.0)	1 (0.2)	1.00
	Parechovirus	1 (0.2)	1 (0.2)	0	1.00

*Coronovirus subtypes; 229E, OC43, NL63, HKU1; RSV; respiratory syncytial virus, PIV; parainfluenza virus, HMPV; human metapneumovirus, INF; influenza, EV; enterovirus.

According to age groups, RV was found to be the most common in the <1 age group (20.1%) (p <0.001) (Figure 2).

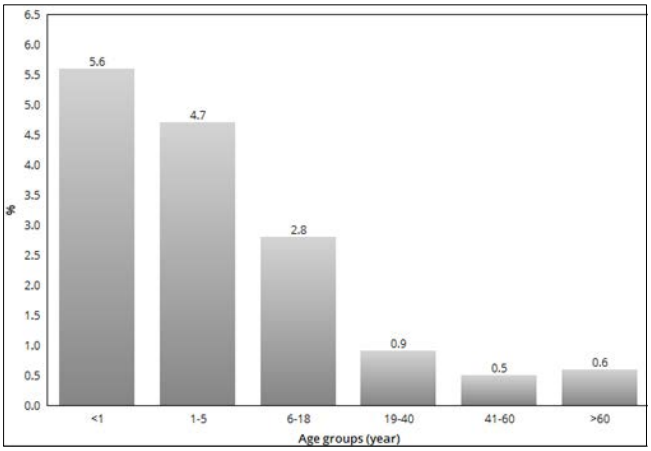

Fig 2: Distribution of rhinoviruses by age groups

The highest positivity rates were found in spring and autumn seasons (p <0.001) (Figure 3).

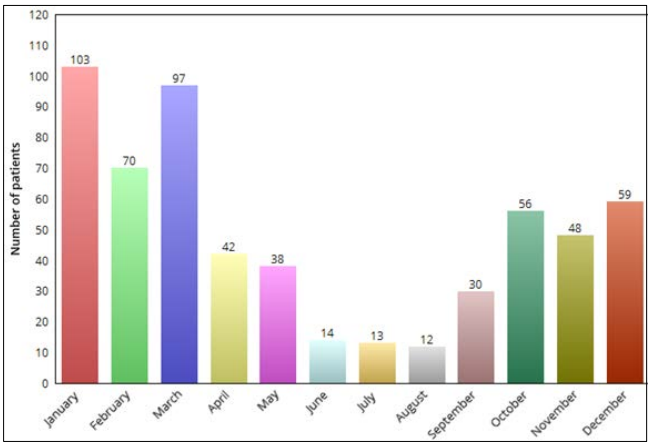

Fig 3: Distribution of rhinoviruses by months

4. Discussion

Viral factors responsible for the etiology of upper and lower respiratory tract infections cannot be identified by clinical symptoms and findings, fort his reason molecular diagnostic methods are needed [13]. Developments in molecular diagnostic methods have revealed the importance of HRV, which is thought to be limited to upper respiratory tract infections, especially in lower respiratory diseases such as asthma, acute exacerbations of chronic obstructive pulmonary disease, cystic fibrosis [14]. The incidence of global HRV varies between regions and from year to year. HRVs are viral pathogens that are the most common cause of respiratory diseases in spring, summer and autumn seasons. RSV and influenza virus are the predominant pathogens in winter [15].

In Turkey, in different studies involving pediatric age group, the HRV positivity of 5.6%, 7.1% and 25.4% have been reported [16-18]. In this study, HRV was found in 15.2% of all age groups in Istanbul. HRV was 18.6% in the pediatric age group and 6.8% in the adult age group and the difference was statistically significant (p <0.001). In studies conducted in different regions of the world, HRV positivity was reported to be 0-52% in the pediatric age group [19,20]. HRV was detected in 2% to 18% of the cases in which respiratory tract viruses were investigated in adults with community-acquired pneumonia [21, 22].

Coinfection with another respiratory tract virus is reported in 7% to 20% of rhinoviral infections. Mixed infections especially in infants cause more severe disease [23-25]. Interestingly, some authors assume that HRV infections can protect the host from more cytopathic respiratory tract viruses through viral interferences with other viruses [23]. In this study, mixed infection was detected in 33.5% of the patients with RV, while the most frequent mixed infection was RSV in the child and adult age group.

In the epidemiology of HRV infections, age is an important factor. Although infections increase significantly in the second year of life, especially in school age, they decrease in advanced age due to antibodies acquired due to previous infections [26]. In our study, the highest rates of positivity were found under 18 years, especially under 1 year. This situation, as stated in some literature; explain the cause of infection at an earlier age due to factors such as nutrition, living in crowded places, socio-economic status and family structure [27].

HRV infections are seen throughout the year. Seasonal changes are observed according to climate type. In the temperate climate of the Northern Hemisphere, the incidence of HRV infections typically peaks in autumn and spring months [28]. Its isolation rate is reported to range from 0% to 70% in different seasons [29]. Infection persists throughout the winter season [30]. It has been shown that HRV infections acquired during the winter months are more severe in the infant population than in the spring and summer months [6]. In autumn, HRVs account for 80-90% of the common cold [31, 32]. In this study, HRV was determined throughout the year, however, the highest rates of positivity were found in spring and autumn.

5. Conclusion

In conclusion, in all age groups, RV was found to be 15.2% in nasopharyngeal swab specimens sent from patients with suspected respiratory tract infections. RV was found to be higher in children (18.6%) than in adults. The most common mixed infection pathogen was RSV. RV positivity rates were highest in spring and autumn. It is epidemiologically important to detect determine the positivity rates of RV and its association with RSV. It is also of great importance especially for children under five years of age in terms of patient follow-up and treatment planning.

Ethics Committee Approval

The study was approved by the Local Ethics Committee with the protocol number of 2018/11/855 was in accordance with the ethical standards established in the Declaration of Helsinki.

Conflict of Interest: None declared.

6. References

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