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The Seasonal Frequency of Viruses Associated With Upper Respiratory Tract Infections in Children

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ARTICLE INFO	A B S T R A C T				
Article type: Original Article	Background: Upper respiratory tract infections (URTI) in children are the most frequent reasons for visiting a family doctor, commonly resulting in inappropriate prescription of antibiotics. In underdeveloped countries a viral respiratory tract infection may be				
Article history: Received: 18 Apr 2012 Revised: 17 July 2012 Accepted: 07 Aug 2012	followed by serious complications. More than 200 viral species are associated with respi- ratory tract diseases in humans and this number is increasing. Objectives: This study was carried out to determine the distribution of common viruses responsible for clinical manifestations of upper respiratory tract infections (URTI) in children throughout the 4 seasons of year.				
Keywords: Epidemiology Child Viruses Respiratory Tract Infection Polymerase Chain Reaction	 Patients and Methods: This cross-sectional study was performed from October 2009 to September 2010 on 2- month and 12- year -old children with clinical manifestations of acute upper respiratory tract infections referring to the outpatient clinics of a children's hospital affiliated to Shahid Beheshti University of Medical Sciences in Tehran, Iran. Nasopharyngeal samples were collected and tested for <i>Influenza virus</i>, <i>Parainfluenza</i>, <i>Adenovirus</i>, <i>Respiratory syncytial virus</i> (RSV), <i>Rhinovirus</i> and <i>Enterovirus</i>, by polymerase chain reaction (PCR). Results: One hundred thirty four out of 330 samples (40.7%) were positive for at least 1 of the tested viruses. <i>Adenovirus</i> was detected with a frequency of 29.9%, followed by <i>Rhinovirus</i> (9%). <i>Adenovirus</i> was more frequent in spring, summer and winter (35%, 22%, and 36.7%, respectively) and <i>Rhinovirus</i> was common in winter (26.7%), followed by spring and autumn (25% each). Frequency of <i>Influenza</i> virus was 22.5% in spring, 15.6% in summer, 21.9% in autumn and 26.7% in winter. The rates of <i>RSV</i> were 9.4%, 15.6%, 12.5% and 13.3%, from spring to winter. <i>Enterovirus</i> was isolated in 7.5% samples in spring, rising to 15.6% in summer, falling to 9.4% and then to 3.3% in cold seasons. <i>Parainfluenza</i> was found 2.5% in spring, 21.9% in summer, 18.8% in the fall and 10% in winter. Conclusions: <i>Adenoviruses</i> are the most commonly detected viruses in childhood URTI. Although frequency of different viruses varies according to the seasons of year, this difference is not significant. 				
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Implication for health policy/practice/research/medical education: This Paper Describes Variations in The Viral Etiology of URTI in Children Useful to Deciding Management Options.

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1. Background

Upper respiratory tract infections (URTI) in children are the most frequent reasons for visiting a family doctor, commonly resulting in inappropriate prescription of antibiotics (1-3). In underdeveloped countries, a viral respiratory tract infection may be followed by serious complications (1). More than 200 viral species are associated with respiratory tract diseases in human and this number is increasing. The relationship between clinical manifestations and causal microorganisms has been reported by various authors but viral detection would provide definite data about the relationship between the clinical picture and specific causative agents (4-6). Specific viral diagnosis may help decrease the use of unnecessary antibiotics (3). Recent studies have shown that some pediatric patients with acute respiratory tract infection become infected simultaneously with multiple respiratory viruses (4, 7, 8). Rhinovirus, Parainfluenza virus, Respiratory Syncytial virus (RSV), and coronavirus play an important role in URTI (1, 2). Since the pattern of causative organisms for respiratory tract infections may vary in different geographical locations, it is important to determine the epidemiology of URTI in a community, in order to plan a rational approach for managing all these very common illnesses in children.

There are few reports from developing countries addressing the issue of viral causes of URTI in all 4 seasons of the year. Previous studies have dealt with specific age groups, hospitalized children, and the infections of the lower respiratory tract (4, 6, 9).

2. Objectives

This study was carried out with the objectives of determining the role of 6 different viruses, namely *Rhinovirus*, *Influenza virus*, *Parainfluenza virus*, RSV, *Adenovirus* and *Enterovirus* in causing upper respiratory tract infection in children during various seasons of year and 2- month to 12 -year-old age groups.

3. Patients and Methods

Children between the ages of 2- month and 12 -year-old with clinical signs and symptoms of URTI referring to the outpatient clinics of Mofid Children's Hospital in Tehran, Iran, from October 2009 to September 2010, were selected for this cross-sectional study during the one -year period of study. We continued carefully the study for 1 whole year so that patients could be evaluated during all the 4 seasons. We selected children consecutively in order to meet our inclusion criteria during each season, until the required number for each season was reached.

Inclusion criteria: Children with at least 2 of the following clinical manifestations of URTI i.e. rhinorrhea, sneezing, sore throat, or cough lasting for < 7 days, with or without fever. Exclusion criteria: the Presence of any of the following signs: tachypnea, chest wall retraction, nasal flaring, asthma, allergy, or an underlying disease involving the cardio-pulmonary system.

After obtaining approval from the ethical committee of the Pediatric Infections Research Center and parental consent, all children were examined by the members of the study team, (pediatricians or pediatric residents) and all relevant findings were documented on a pre-designed questionnaire. Nasopharyngeal swabs were taken from the patients of the study and sent to the laboratory in VTM transitional median ice bags where they were stored at- 70°C and the different viruses were identified by the PCR method (10).

The used primers for identifying the viruses were as follows:

Influenza/Forward: 5-CAGAGACTTGAAGATGTC-3

Influenza/reverse: 5-CGATCAAGAATCCACAATAAGTGCAA-GATCCCAATAATA-3

RSV/Forward: 5-GGAACAAGTTGTTGAGGTTTATGAATATGC-3 RSV/reverse: 5-CTTGACTTTGSTAAGAGCCATTCT-3 Adenovirus/Forward: 5-CCCTGGTA(GT)CC(AG)AT(AG)TTGTA-3 Adenovirus/Reverse: 5 GACTC (ct) TC(AT)GT(GC)AG(CT)GGCC-3 Rhinovirus/Forward: 5-GCACTTCTGTTTCCCC-3 Rhinovirus/Reverse: 5-CGGACACCCAAAGTAG-3 Parainfluenza/Forward: 5-CTTTGGGAGTTGAACAAACAGTT-3 Parainfluenza/Reverse: 5-CTCGAGGTTGTCAGGATATAG-3 Enterovirus/Forward: 5-CATGGTGAGAAGAGTCTATTGAGCTA-3 Enterovirus/Reverse: 5-GGACACCCAAAGTAGTCGGTTC-3

Frequency of each virus for URTI in children was presumed to be 5% and the sample size was determined to be 292 patients.

Statistical analysis was done by SPSS software, and the frequency of different viruses in different age groups, seasons and both genders was determined.

4. Results

A total of 330 children with acute URTI (61.2% males) were included, 80 patients in the fall, 90 in winter, 80 in spring and 80 in summer. One-hundred and thirty-four samples were positive for at least 1 of the tested viruses. 63 (47%) of these patients were 2 > years old, 48 (35.8%) between 2-5 years old and 23 (17.2%) were > 5 years old. Clinical manifestations of the respiratory infection in children with a detectable viral pathogen were as follows:

96.9% of the patients had coryza, 84.0% cough, 71.6% fever and 17.2% sore throat.

Frequency of different viruses detected in the 134 positive samples was as follows:

Adenovirus 30%, Rhinovirus 23%, Influenza virus 22%, Respiratorysyncytial virus 13%, Para influenza virus 13% and Entero virus 9.0% (Figure 1).

Adenovirus was the most commonly isolated pathogen in infants and toddlers, *Rhinovirus* and *Influenza virus* were more frequent in children aged 5 < years, (*Table* 1). More than 1 virus were detected in 12 specimens, 3 of these had been collected from children < 2 years old, 7 from preschoolers between 2-5 years of age and 2 samples from school children > 5 years old (*Table* 1).

As depicted in *Table 2*, fever was commonly present in most infections except for *Enterovirus*, while sore throat was a predominant symptom in infections with *Influenza virus* and *Rhinoviruses*.

Frequency of different pathogens during different seasons is shown in *Figure 2*.

5. Discussion

In our study, with a population of 330 children with URTI, specific etiologic agents were identified in 134 (40.7%) patients. The identification frequency of etiological agents in children with acute respiratory infections varies widely with geographical location and viral isolation techniques. Lin's study from Taiwan quoted a figure of 40% and in children hospitalized with ARI in Korea, a specific viral agent was identified in 25% of nasopharyngeal aspirates rates (5, 6). Authors from Western India reported the detection of a viral antigen in 37.1% of 385 children with respiratory tract infections (11). In a study on young Finnish children under the age of 4 years with acute symptoms of URTI lasting for < 48 hours, a viral etiological

Table 1. Frequency of Different Viruses According to Different Age Groups								
Virus Type	< 2 y (n = 63)		2-5 y(n=48)		>5 y (n=23)			
	No.	%	No.	%	No.	%		
Influenza virus	9	14.3	14	29.4	6	26.1		
Parainfluenza virus	7	11.1	7	14.6	3	13		
Adenovirus	22	34.9	15	31.3	3	13		
Rhinovirus	11	17.5	14	29.2	6	26.1		
RSV	7	11.1	5	10.4	5	21.7		
Enterovirus	10	15.9	0		2	8.7		
Total virus types detected	66		55		25			
Abbraviation: DSV: respiratory supertial virus								

Abbreviation: RSV; respiratory syncytial virus

Table 2. Relationship Between Pathogens and Clinical Manifestations (n=134)

	Manifestations, %				
Viruses	Cough	Coryza	Fever	Sore Throat	
Influenza virus	22.1	21.3	20.8	30.4	
Para influenza virus	12.4	11.8	14.6	21.7	
Adenovirus	31	29.9	31.3	17.8	
Rhinovirus	22.1	22.8	22.9	30.4	
RSV	13.3	12.6	10.4	17.4	
Enterovirus	8	9.4	9.4	0.0	





Figure 1. Frequency of Different Viruses Detected in Nasopharyngeal Swabs of Children With URTI in 2009-2010

agent was discovered in 92% (7). In other study on young adults, the virus detection rate for acute respiratory infections was almost 70% (12). However, a study that tested for the presence of *Adenovirus, Influenza virus* and RSV by rapid chromatography detected one of the three viruses in 16% of throat swabs in children aged between 3 months and 15years with URTI referring to the outpatient clinics of a children's hospital affiliated to Shahid Beheshti University of Medical Sciences in Tehran (13).

Although our viral detection rate was higher than some of the studies from South East Asia, it was considerably lower than the Finnish study; this could be due to the fact that we did not test for the presence of corona virus



Figure 2. Frequency of Different Pathogens During Different Seasons of the Year

which has been reported as a common cause of mild URTI in children in various studies (1, 2, 7). In our study, most frequent causes of URTI were Adenovirus (30%), Rhino virus (23%), and Influenza virus (22%). In Rouhola's study Rhino virus was found to be the most common agent detected in71% of children, while Adenovirus was only found in 12% and Enterovirus in 10% (7). In a study performed in Iran, Adenovirus was the most common pathogen causing URTI among subjects (13).

As we had expected, we found that the frequency of *Adenovirus* was 36.7% in winter and entero viral infection was the most common in summer and the least common in winter. The seasonality of respiratory viruses has been reported in other studies as well, especially in temperate climates; *Influenza* and RSV were more prevalent in winter and *Rhinoviruses* in spring and the fall (14). In Barati's study, *Influenza virus* was more commonly isolated in winter and RSV in spring and the fall, but *Adenovirus* did not follow a specific seasonal pattern (13). In addition, no seasonal variation was found in the prevalence of *Adenovirus* in children with acute respiratory infection in Taiwan (5). Some authors from the tropical regions have reported a higher prevalence of RSV infection in rainy seasons (15).

RSV was the third common viral pathogen in children aged > 5 years after *Influenza virus* and *Rhinovirus* in our study. Most viral pathogens (47%) were detected in young children < 2 years and the most common virus was Adenovirus, detected in 34.9% of cases. In our study, Entero virus was not isolated in 2-5-year-old ones with URTI. The unexpected low rate of RSV in our patients with lower ages can be explained by the fact that our samples were collected from the outpatient clinics as young children with RSV infection got very ill, they usually needed to be admitted to hospitals (11, 14, 15). RSV was isolated from 73% of 178 young children < 5 years old admitted with acute respiratory infection in Sao Paulo, Brazil and from the majority of hospitalized young children in India but only 13% of their OPD patients (11, 16). In some studies, RSV was the most common pathogen detected from the respiratory tract of children with respiratory tract infections, but in Lin's study, RSV was the least common organism found in URTIs in children (5, 6, 17, 18).

Infections with 1 < virus were detected in 12 of our subjects; only three of these were 2 > years. Concomitant presence of multiple viruses was noted in Rouhola's study as well. In26% of their under study subjects, 2 viruses were detected while in 6%, 3 or 4 viruses were isolated from the nasopharyngeal aspirates (7). Co-infection with multiple viral agents has also been reported in children hospitalized with lower respiratory tract infections in China; similar to our study in which a higher frequency of simultaneous infection with two viruses was noticed in the 2-5 year age group (4), the highest prevalence of co-infection with two or more viruses was in the3-6 year age group (4). The reason might be higher possibility of contact with other children in day-care centers and other places.

The results of this study demonstrate that *Adenovirus* and *Rhinovirus* were the two most common viruses isolated from pediatric outpatients with acute URTIs; *Adenovirus* was more frequent in spring and winter and coryza and cough were the most common symptoms. On the whole, the percentage of boys with viral URTI was higher than girls, but in this study *Adenovirus* infection was more common in females.

Findings of this study delineate the epidemiology of upper respiratory tract infections in children during different seasons of year and help plan strategies for prevention from and treatment of URTIs and make health personnel aware of the ineffectiveness of antibiotics in the management of URTIs.

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Authors' Contribution

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