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Egyptian Pediatric Association Gazette

journal homepage: www.elsevier.com/locate/epagPrevalence of Human rhinovirus infection in young children with acute wheezing[☆]Hanaa I. Rady^{a,*}, Amani El Kholy^b^a Department of Pediatrics, Faculty of Medicine, Cairo University, Cairo, Egypt^b Department of Clinical and Chemical Pathology, Faculty of Medicine, Cairo University, Cairo, Egypt

ARTICLE INFO

Article history:

Received 6 March 2018

Accepted 4 May 2018

Available online 8 May 2018

Keywords:

Asthma

Rhinovirus infection

Wheezes

ABSTRACT

Introduction: Recurrent wheezing is one of the leading causes of chronic illness in childhood. We aimed to evaluate the prevalence of Human Rhinovirus (HRV) infection in the acute attack of wheezy chest which began after a respiratory illness.

Methodology: The study was conducted on 200 children aged 2 months to 5 years presenting to the emergency department with an acute wheezy episode either for the first time or recurrent wheeze defined as >2 reports of wheezing in the first 3 years of life. All subjects were subjected to a complete history and clinical examination. Chest X-ray was done to all subjects. Nasopharyngeal and oropharyngeal swabs were obtained from all subjects and the presence of HRV was determined by PCR examination.

Results: By PCR method, 163 patients (81.5%) were positive for viral infection. Due to viral co-infection, 49.5% (99 cases) were +ve for Respiratory Syncytial virus followed by HRV 43.5% (87 cases).

Conclusion: HRV was the second common viral infection in children with wheezes. Its prevalence was more in winter with higher incidence of recurrence. Compared to the other respiratory viruses, it had the higher mortality 43.7%.

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Introduction

Asthma is a heterogeneous and multi-factorial disease that manifests as episodes of coughing, wheezing, and shortness of breath mainly at night.¹ The major pathophysiology of asthma is bronchial inflammation with airway hyper-responsiveness, which results in reversible airway obstruction.²

Among the various factors that have been involved in the pathogenesis of asthma, viral infections are the most prominent. Viral infection affects wheezing and asthma in children and adults of all ages. Wheezing illnesses are usually viral in origin, and children with more severe wheezing episodes are more likely to develop asthma later on in their life.³

Human rhinoviruses (HRV) are not only the main pathogens responsible for the common cold, but are also now recognized to have a major impact on asthma pathogenesis. Children who experience repeated rhinovirus-induced wheezing episodes in infancy have a significantly increased risk of developing asthma, even

when compared to children who experience wheezing induced by respiratory syncytial virus (RSV).⁴

The aim of this study was to determine the prevalence of Human Rhinovirus as a cause of acute wheezing in Egyptian children after an acute respiratory illness.

Methodology

Patients' inclusion criteria

A prospective study including children aged 2 months to 5 years presenting to the emergency department (ED) of Cairo University Children Hospitals, with an acute wheezy episode (signs of respiratory distress and expiratory wheezes on auscultation and/or hyperinflation of the chest on chest radiograph) either for the first time or recurrent wheeze defined as >2 reports of wheezing in the first 3 years of life.

Patients' exclusion criteria

We excluded children with underlying cardiac or chronic pulmonary disease (other than asthma), the presence of stridor or

[☆] The work was performed at Cairo University Children's Hospitals, Cairo, Egypt. Peer review under responsibility of Egyptian Pediatric Association Gazette.

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daily treatment with oral corticosteroids for >2 days prior to presentation.

All included cases had complete physical examination including grades of respiratory distress chest X-ray and laboratory investigations in the form of oxygen saturation, blood gases, and complete blood count. A nasopharyngeal and oropharyngeal swabs were taken and reverse transcription PCR was used to screen the samples for HRV.

Swabbing

- Oropharyngeal swabbing: a dry sterile tip flocced with nylon fiber swab applicator was used to swab both the tonsils and the posterior pharynx.
- Nasopharyngeal swabbing: a flexible sterile nylon fiber swab applicator was inserted into the nostril and back to the nasopharynx. It was then slowly withdrawn with a rotating motion.
- Sample processing: The swabs were placed in a 15 ml centrifuge tube labeled with the patient unique ID and containing 2 ml viral transport media (VTM: consisting of a sterile solution of bovine albumin fraction V, HEPES buffer, penicillin, and streptomycin in HANK's balanced salt solution). The received swabs inside the 15 ml tube were agitated vigorously for 10 s using a vortex mixer to free cells from the swab tip, and then both swabs were removed from the tube and discarded using a forceps. The sample was kept in a –80C deep freezer until processed.
- Nucleic acid extraction: Automated extraction was performed using the QiAcube machine with QIAamp® Viral Mini Kit cat# 52904, 52906 (QIAGEN) using the manual lysis protocol which consists of purification from manually lysed cell-free body fluids. Multiplex Real-time PCR was performed using the Anyplex™ II RV16 Detection cat# RV7G01Y from Seegene Inc, compatible with CFX96™ Real-time PCR Bio-Rad, the interpretation was done using the see gene viewer program.

Management of patients was followed depending on their condition whether received ambulatory therapy, required hospital admission or required intensive care unit admission. We recorded the length of hospital stay and patient's outcome: discharged, transferred or died.

Table 2
Demographic and clinical data of all studied cases (n = 200).

Variable		HRV (+ve)n = 87	HRV (–ve)n = 113	P value
Age (Months) (Median Range)		14 (5–48)	16 (5–72)	0.001
Sex	Male	n(%) 51(58.6%)	71(62.8%)	0.545
	Female	n(%) 36(41.4%)	42(37.2%)	
Cough	Positive	n(%) 62(71.3%)	108(95.6%)	0.001
	Negative	n(%) 25(28.7%)	5(4.4%)	
Wheezes	Positive	n(%) 62(71.3%)	93(82.3%)	0.064
	Negative	n(%) 25(28.7%)	20(17.7%)	
Tachypnea	Yes	n(%) 58(66.7%)	87(77%)	0.105
	No	n(%) 29(33.3%)	26(23%)	
Grunting	Yes	n(%) 49(56.3%)	97(85.8%)	0.001
	No	n(%) 38(43.7%)	16(14.2%)	
Cyanosis	Yes	n(%) 33(37.9%)	27(23.9%)	0.032
	No	n(%) 54(62.1%)	86(76.1%)	
Fever	Positive	n(%) 73(83.9%)	94(83.2%)	0.891
	Negative	n(%) 14(16.1%)	19(16.8%)	
Rhinorrhoea	Positive	n(%) 25(28.7%)	20(17.7%)	0.064
	Negative	n(%) 62(71.3%)	93(82.3%)	
Vomiting	Positive	n(%) 58(66.7%)	81(71.7%)	0.445
	Negative	n(%) 29(33.3%)	32(28.3%)	
Diarrhea	Positive	n(%) 42(48.3%)	54(47.8%)	0.581
	Negative	n(%) 45(51.7%)	59(52.2%)	

HRV: Human Rhinovirus.

The study was explained for each parent before inclusion and an informed written consent was obtained from parents before enrollment.

Statistical analysis

Statistical package for social science (SPSS) version 9.0 was used for analysis of data. Data were summarized as mean, SD and percentages. Non parametric (Mann-Whitney U) test was used for analysis of quantitative data, as data were not symmetrically distributed. While Chi square test was used for detection of risk factor for Rhinovirus infection. p value was considered significant if <0.05.

Results

We studied 200 children that presented to Children Hospital of Cairo University ED with acute wheezy chest. The patients' condition varies from requiring nebulizer at the ED, hospital admission and oxygen supplementation to pediatric intensive care admission for infusion therapies or mechanical ventilation.

The studied patients were 122 male and 78 female aged 2 months to 5 years. By PCR method, 163 patients (81.5%) were positive for viral infection and 37 (18.5%) patients were negative. From the 163 viral infected patients 56 patients (34.4%) had single infection, while 107 patients (65.6%) had co-infection with more than one virus. RSV affected 49.5% (99 cases), followed by HRV 43.5% (87 cases) (Table 1).

All the demographic and clinical data of cases were demonstrated in Table 2. The median age of patients who were positive

Table 1
Distribution of Viral infection among studied cases (n = 200).

Variable	Frequency	Percent
Respiratory Syncytial Virus	+ve 99	49.5%
Human Rhinovirus	+ve 87	43.5%
Adenovirus	+ve 81	40.5%
Metapneumovirus	+ve 43	21.5%
Coronavirus 229E	+ve 42	21%

Co-infection with more than one virus was much more common (83.5%, 79 cases) than infection with single virus (16.5%, 8 cases) among rhinovirus positive patients.

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