Burden, seasonal pattern and symptomatology of acute respiratory illnesses with different viral aetiologies in children presenting at outpatient clinics in Hong Kong

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Abstract

Respiratory viruses cause acute respiratory diseases with a broad and overlapping spectrum of symptoms. We examined the clinical symptoms and explored the patterns of various respiratory viral infections in children in Hong Kong. Among 2090 specimens collected from outpatient care (2007–2010), 1343 (64.3%) were positive for any virus by the xTAG assay, and 81 (3.9%) were positive for co-infection. The most frequently detected viruses among children aged 6–15 years were enterovirus/rhinovirus and influenza virus A, whereas most non-influenza viruses were more frequently detected in younger children. Higher body temperature was more common for illnesses associated with influenza viruses than for those associated with non-influenza viruses, but other symptoms were largely similar across all infections. The seasonality pattern varied among different viruses, with influenza virus A being the predominant virus detected in winter, and enterovirus/rhinovirus being more commonly detected than influenza virus A in the other three seasons, except for 2009.

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Introduction

Acute respiratory illness (ARI) represents an important cause of hospitalization and death in all age groups worldwide [1]. Although ARIs can be caused by a wide range of different respiratory viral pathogens, ascertainment of the exact causative agents is rarely clinically indicated, and is thus not routinely performed. Among the small proportion of patients needing hospitalization, significant disease burdens have been attributed to adenovirus (AdV) in children, respiratory syncytial virus (RSV) and influenza virus A (IFVA) in all age groups, and rhinovirus (RhV) and parainfluenza virus 3 (PIV 3) in children and the elderly [2]. However, the full spectrum of disease burden among the majority of patients with ARIs presenting in community outpatient settings has remained largely elusive. Seasonal patterns of ARIs caused by influenza virus [3] and RSV [4] have been better described in some geographical areas, but those of most other respiratory viruses remain poorly understood.

The generally overlapping spectrum of non-specific symptoms makes it very difficult to distinguish between infections with different respiratory viruses [5]. A better understanding of their differential symptom patterns may help to identify cases that are more likely to be influenza virus infections, and thus may benefit clinically from specific antiviral treatment.

The Hong Kong Special Administrative Region is situated in the northern hemisphere, and has a subtropical climate, with an

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annual variation in temperature from 14.5–18.9°C in January and February to 26.2–31.4°C in June and July, and a mean relative humidity from 69–74% in December and January to 83% in March and April. In this study, we aimed to investigate the burden of ARIs caused by different respiratory viral pathogens among children aged ≤15 years in a community outpatient setting, to describe their seasonal patterns of occurrence, and to characterize their clinical characteristics at presentation.

Materials and methods

Sources of data

As part of a larger study on transmission of influenza viruses in households, we recruited patients from primary-care outpatient clinics in private and public sectors across Hong Kong who met our inclusion criteria, including: (a) being a Hong Kong resident; (b) presenting with at least two symptoms of ARI, including a body temperature of ≥37.8°C, headache, sore throat, cough, runny nose, sputum, and myalgia; (c) onset of symptoms within the preceding 48 h; and (d) living in a household with at least two other people, none of whom had reported ARI in the preceding 14 days. All consenting subjects completed a short data collection form, and had two sets of pooled nasal and throat swab specimens collected by a trained nurse. One specimen was stored immediately in viral transport medium for subsequent virological testing; the other specimen was tested on site with the QuickVue Influenza A + B rapid diagnostic test (Quidel, San Diego, CA, USA). Subjects with a positive rapid test result and their household contacts were further followed up [6], but, in the present analysis, we also analysed laboratory results from the other specimen from all subjects, regardless of their rapid test result. Proxy written informed consent was obtained for all participants from their parents or legal guardians, with additional written consent being obtained from those aged 8–16 years. The study protocol was approved by the Institutional Review Board of Hong Kong University. Weekly meteorological data, such as temperature, humidity, and precipitation, were obtained from the Hong Kong Observatory.

Laboratory methods

Each pooled nasal and throat swab specimen was stored in viral transport medium (5% bovine serum albumin in Earle's balanced salt solution with antibiotic), kept at 2–8°C immediately after collection, and cryopreserved at −70°C within 36 h. The specimens were tested for eight common respiratory viruses (including types and subtypes), namely IFVA (subtypes H1 and H3), influenza virus B (IFVB), RSV (subtypes A and B), PIV (types 1–4), metapneumovirus (MPV), enterovirus (EnV)/RhV, AdV, bocavirus (BoV), and coronavirus (CoV) (types NL63, HKU1, 229E, and OC43), with the xTAG RVP FAST version 2.0 multiplex assay (Luminex Molecular Diagnostics, Toronto, Ontario, Canada), and this was followed by product detection and identification with a Luminex suspension microarray [7]. Total nucleic acid was extracted from the clinical specimens with the NucliSens easyMAG extraction system (bioMerieux, Zaltbommel, The Netherlands), according to the manufacturer's instructions. The extracted nucleic acid was tested for respiratory viruses.

Statistical analysis

Detection rates (and co-detection rates for co-infection) of each virus, stratified by age group (0–5 years and 6–15 years), were calculated by dividing the number of specimens positive for the corresponding virus by the total of positive specimens in that age group. Symptomatology was examined by comparing clinical symptoms of different respiratory virus infections by the use of Pearson's chi-square test (χ^2) or Fisher's exact test (FE). Logistic regression was used to examine the association of different symptoms with influenza or non-influenza virus infection. To assess the seasonal pattern, percentages of different positive specimens across different seasons were compared by use of the chi-square test or FE. Here, we defined winter as December to February, spring as March to May, summer as June to August, and autumn as September to November. Also, logistic regression was used to assess the association between virus detection and meteorological factors, including temperature, absolute humidity, and precipitation. All statistical analyses were performed with R version 2.15.0 (R Foundation for Statistical Computing, Vienna, Austria).

Results

A total of 2090 swab samples were obtained from children aged ≤15 years from February 2007 to December 2010 (187, 1224, 570 and 109 in 2007, 2008, 2009 and 2010, respectively). The detection rate was significantly different across the 4 years, with the highest rate being in 2009, which might due to the pandemic H1N1 IFVA. There was no difference in sex distribution across the years, whereas there was a significant difference in age group percentage across years, with a higher percentage of children in the older age group (6–15 years) than in the younger age group (<6 years) for the first 3 years (2007–2009) but not for 2010 (Table S1).

There were 1343 (64.3%) specimens positive for at least one of the respiratory viruses, 81 (3.9%) specimens positive for more than one respiratory virus, and two specimens positive