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## Original article

# Clinical relevance of rhinovirus infections among adult hospitalized patients



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## ABSTRACT

Human rhinovirus (HRV) is an emerging viral pathogen.

**Aim:** To characterize a group of patients admitted due to infection by this agent in a general hospital in Chile.

**Methods:** Cases were identified by RT-PCR for 1 year through active surveillance of patients admitted with severe respiratory illness. Diagnosis was not available during hospitalization. Thirty-two cases were identified, 90% were  $\geq 60$  years old or had co-morbid conditions. Human rhinovirus-related admissions represented 23.7% of hospitalization due to severe acute respiratory infections among adults and ranked second to influenza (37.8%). Patients presented with pneumonia (68.8%), decompensated chronic lung conditions (21.9%), heart failure or influenza-like illness (6.3% each). Admission to intensive or intermediate care units was required by 31.2% and in-hospital mortality reached 12.5%. A CURB-65 score  $\geq 3$  was significantly associated to in-hospital mortality ( $p < 0.05$ ). Most patients received antibiotics (90%).

**Conclusions:** Human rhinovirus infections in elderly patients with co-morbid conditions are associated with hospitalizations, requiring critical or semi-critical antibiotics use. A high CURB-65 score was associated to in-hospital mortality.

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## Introduction

Upper and lower viral respiratory infections represent an important global health burden for adult patients due to

their morbidity, absenteeism, outpatient medical visits, hospitalizations, mortality, and inappropriate antibiotic use.<sup>1–9</sup> Human rhinovirus is one of the etiological agents involved in acute respiratory infections and has been associated with crisis of asthma, exacerbated chronic bronchitis, bronchiolitis

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and pneumonia in children.<sup>10</sup> Nonetheless, its role in adult patients is less accepted despite progressive evidence of its importance in outpatient clinical settings<sup>4,11,12</sup> or in hospitalized or immunosuppressed patients.<sup>13,14</sup> This unrecognized role is changing after the recent availability of molecular diagnostic testing that has enhanced our knowledge on this viral agent.<sup>2,3,15,16</sup>

In this work we report seasonality, clinical features and outcomes of adult patients hospitalized during 1 year for severe respiratory acute infection secondary to human rhinovirus infection in a general hospital.

## Patients and methods

### Study design and setting

The Hospital Militar of Santiago is one of the six active surveillance centers for acute severe respiratory infections requiring admission, a system launched in July 2011 by the Pan American Health Organization (PAHO) and the Chilean Ministry of Health after the influenza A (H1N1) pandemic to recognize new respiratory viral threats. It attends active and retired military personnel and their relatives. The average age of admitted patients is 76 years.

This was a prospective descriptive study that included all adult patients  $\geq 18$  years admitted due to severe acute respiratory infection (SARI) associated with a confirmed human rhinovirus detection obtained from respiratory samples during the year 2012 (see below). SARI was defined by the presence of fever and respiratory symptoms associated either with tachypnea ( $\geq 30 \text{ min}^{-1}$ ) or a low digital pulse oxymetry ( $< 90\%$ ) at room air.<sup>17</sup> All patients fulfilling these criteria were reported on-line to a centralized surveillance system and nasopharyngeal swab samples are assessed, at local level, for the presence of influenza A-B, respiratory syncytial virus, parainfluenza 1, 2, and 3, adenovirus and human metapneumovirus by indirect immunofluorescence using commercial reagents. Influenza A or B positive samples as well as all negative samples were referred to a reference laboratory (*Instituto de Salud Pública: ISP*) for further analyses using molecular techniques. Influenza virus was tested and sub typed with the molecular kit FluRUO-01, and non-influenza respiratory viruses using kit KK0812, provided by the CDC. The latter allows detection by PCR of adenovirus, respiratory syncytial virus, human metapneumovirus, parainfluenza 1, 2, and 3, as well as rhinovirus (HRV), not included in the initial immunofluorescence panel.<sup>18</sup> For nucleic acid extraction we used the automated Easy Mag system from Biomerieux. Amplification was performed using Ag Path -ID kits from Ambion and a real time thermo cycler (Applied Biosystems). The results of a positive HRV detection were not available during hospitalization.

Cases were analyzed according to demographic information, seasonality, comorbidities, clinical presentation including chest X-ray, PaFiO<sub>2</sub>, and outcome at the moment of discharge. Some topics were collected prospectively (demographics, comorbidities, vaccine history, tobacco smoking, place of hospitalization) and other retrospectively (clinical presentation and symptoms, laboratory data, management,

severity score and outcome). Respiratory failure was defined as a PaFiO<sub>2</sub>  $< 300$  and graded.<sup>19,20</sup>

### Statistical analysis

Results are shown in a descriptive manner. Factors associated to mortality were identified calculating odds ratios (OR) with their respective confidence intervals. Two severity scores (CURB-65 and CAP-PIRO) were calculated and compared to predict in-hospital mortality.<sup>21,22</sup>

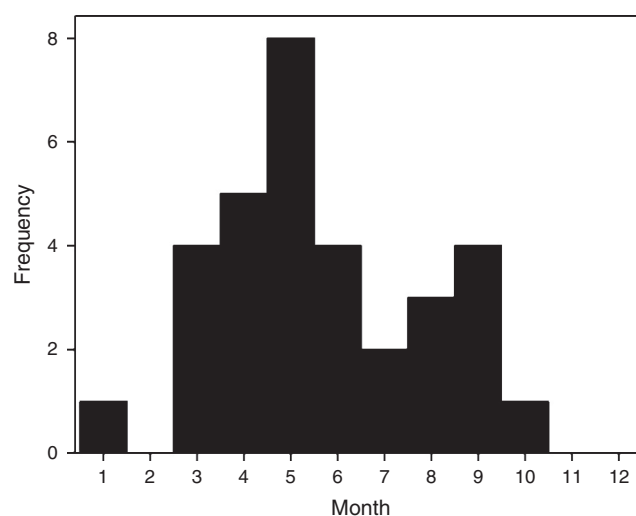
## Results

Thirty-two confirmed patients, each with a single severe episode of HRV infection were admitted during 2012. Cases presented a seasonal pattern along the year but were detected continuously during 8 months from March to October (summer to spring in southern hemisphere) (Fig. 1). Of 135 adult patients admitted with SARI during year 2012 with a confirmed viral etiology, HRV ranked second only to influenza infections (23.7% versus 37.8% for influenza).

Mean age was elevated (79.5 years) and 90% were older than 60 years (Table 1). Only two patients lived in a long-term care facility, but near 20% were bedridden. Over 50% of the patients had two or more comorbidities, mainly chronic pulmonary conditions, heart disease, diabetes mellitus, or neurologic diseases. Cancer, morbid obesity, or kidney disease were not common. No case was associated with chronic liver disease and only one patient was immunosuppressed. Previous tobacco smoking affected near a third of this population and current smoking was still admitted by two out of 32 patients. Almost one-third of patients with chronic lung disease were domiciliary oxygen users (Table 1).

### Clinical manifestations

Most patients were admitted under the diagnosis of community-acquired pneumonia, followed by chronic



**Fig. 1 – Monthly distribution of 32 patients admitted with human rhinovirus-associated severe acute respiratory infection during one year at a general hospital in Chile.**

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