

## Retrospective Study

## Prevalence of adenovirus and rotavirus infection in immunocompromised patients with acute gastroenteritis in Portugal

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**Author contributions:** Almeida S and Baldaque I performed the experimental tests for Adv and RV detection; Ribeiro J, Ferreira D, and Arrabalde C were responsible for the data collection; Ribeiro J and Sousa H analyzed data; Ribeiro J and Ferreira D wrote the paper; Sousa H supervised the study; all authors have provided the final approval of the manuscript.

**Conflict-of-interest statement:** All authors declare no conflicts of interest with any competing financial interest for the work described in this paper.

**Data sharing statement:** Not applied.

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Received: May 8, 2015

Peer-review started: May 9, 2015

First decision: June 3, 2015

Revised: September 9, 2015

Accepted: September 29, 2015

Article in press: September 30, 2015

Published online: November 12, 2015

### Abstract

**AIM:** To characterize the prevalence of rotavirus (RV) and adenovirus (AdV) infections in immunocompromised patients with acute gastroenteritis.

**METHODS:** The presence of RV and AdV (serotypes 40 and 41) was evaluated in 509 stool samples obtained between January 2009 and December 2010 from 200 immunocompromised patients (83 females and 117 males; median age 21 years old, range 0-72). The diagnosis of infection was performed as a routine procedure and the presence of RV and AdV (serotypes 40 and 41) was determined by immunochromatography using the RIDA® Quick Rota-Adeno-Kombi kit (r-Biopharm, Darmstadt, Germany). The data analysis and description of seasonal frequencies were performed using computer software IBM® SPSS® (Statistical Package for Social Sciences) Statistics version 20.0 for Mac. The frequencies of infection were compared into different age and gender groups by  $\chi^2$  test.

**RESULTS:** The study revealed 12.4% AdV positive samples and 0.8% RV positive samples, which correspond to a prevalence of 6.5% and 1.5%, respectively. AdV was more frequent between October 2009 and April 2010, while RV was identified in April 2010 and July 2010. The stool analysis revealed that from the 509 samples, 63 (12.4%) were positive for AdV and 4 (0.8%) positive for RV, which by resuming the information

of each patient, lead to an overall prevalence of AdV and RV of 6.5% (13/200 patients) and 1.5% (3/200 patients), respectively. The stratification of the analysis regarding age groups showed a tendency to an increased prevalence of infection in paediatric patients between 0-10 years old. Considering the seasonal distribution of these infections, our study revealed that AdV infection was more frequent between October 2009 and April 2010, while RV infection was characterized by two distinct peaks (April 2010 and July 2010).

**CONCLUSION:** The overall prevalence of AdV and RV infection in immunocompromised patients with acute gastroenteritis was 8% and AdV was the most prevalent agent.

**Key words:** Viral gastroenteritis; Adenovirus; Rotavirus; Immunocompromised host; Stool samples

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**Core tip:** Acute gastroenteritis has been associated with significant rates of morbidity and mortality among immunocompromised patients. Rotavirus (RV) and adenovirus (AdV) are described as common agents of viral gastroenteritis causing acute diarrhoea. This is the first study in Portugal to characterize the prevalence and seasonal features of RV and AdV infections in immunocompromised patients with acute gastroenteritis. Results revealed 12.4% AdV positive samples and 0.8% RV positive samples, which correspond to a prevalence of 6.5% and 1.5%, respectively. Our results also demonstrate the importance of to add more screening methods for other emergent enteric viruses, in order to avoid the morbidity and mortality of the immunocompromised patients.

Ribeiro J, Ferreira D, Arrabalde C, Almeida S, Baldaque I, Sousa H. Prevalence of adenovirus and rotavirus infection in immunocompromised patients with acute gastroenteritis in Portugal. *World J Virol* 2015; 4(4): 372-376 Available from: URL: <http://www.wjgnet.com/2220-3249/full/v4/i4/372.htm> DOI: <http://dx.doi.org/10.5501/wjv.v4.i4.372>

## INTRODUCTION

Acute gastroenteritis, one of the main causes of morbidity and mortality in the world, is a consequence of microbial infections, which in industrialized countries are mainly caused by viruses, such as rotavirus (RV), enteric adenovirus (AdV), astrovirus and human calicivirus<sup>[1-3]</sup>.

RV is the most common cause of severe diarrhoea in children under 5 years of age, adults in close contact with infected children, hospitalised patients and the elderly<sup>[3,4]</sup>. Data from United States reveal that RV infection is responsible for approximately 3 million cases of acute diarrhoea in children each year<sup>[5]</sup>. RV infection is associated with high rates of morbidity throughout

the world and high rates of mortality in developing countries, where gastroenteritis caused by RV account for more than 800000 deaths per year due to poor nutrition and lack of health care<sup>[6]</sup>. In the majority of countries, RV infections occur dispersed throughout the year, nevertheless in temperate climates is characterized by a peak during the winter months<sup>[1-3]</sup>.

AdV, especially serotypes 40 and 41 (enteric AdV), are frequently related with high morbidity and mortality in immunocompromised patients with the most susceptible groups to be children and patients submitted to transplantation<sup>[7-9]</sup>. Enteric AdV have been related with acute diarrhoea in variable frequency (ranging from 1.4% to 10%), depending on the geographic location and type of patients<sup>[10,11]</sup>. AdV is known for its large distribution worldwide and the majority of the studies refer it to be equally distributed during all the seasons of the year<sup>[8,9]</sup>.

Immunocompromised patients constitute an important group for prevention of gastrointestinal infections<sup>[7,12,13]</sup>. In fact, the incidence of infection-related post-transplant diarrhoea has been reported to be up to 40%, with viruses being the most common pathogens<sup>[2,3,12]</sup>. Considering the importance of gastroenteritis prevention in immunocompromised individuals, the diagnosis of AdV and RV at early stages of the disease is extremely important, in order to reduce morbidity and mortality.

The aim of this study was to characterize the prevalence of RV and AdV infection in immunocompromised patients with acute gastroenteritis from the North region of Portugal treated at the Portuguese Institute of Oncology of Porto.

## MATERIALS AND METHODS

### Population

This study was performed as a cross-sectorial retrospective hospital-based case study with 509 stool samples obtained between January 2009 and December 2010 from immunocompromised patients diagnosed with acute diarrhoea at Portuguese Institute of Oncology of Porto (IPO Porto). Samples were obtained from 200 immunocompromised patients with different haematological malignancies (median age 21 years old, range 0-72): 83 female (median age 15 years old, range 0-65) and 117 male (median age 39 years old, range 0-72).

### RV/AdV detection

The diagnosis of infection was performed as a routine procedure at the Virology Service of IPO Porto. The stool specimens were tested as soon as possible after collection and the presence of RV and AdV (serotypes 40 and 41) was determined by immunochromatography using the RIDA® Quick Rota-Adeno-Kombi kit (r-Biopharm, Darmstadt, Germany) according to manufacturer instructions. The faecal samples were diluted in the dilution buffer supplied with the kit. This is a ready-to-use test based on a nitrocellulose membrane sensitized with

**Table 1 Adenovirus and rotavirus results discriminated by year n (%)**

	AdV positive	RV positive	Negative
Total (n = 509)	63 (12.4)	4 (0.8)	442 (86.8)
Year 2009 (n = 189)	24 (12.7)	-	165 (87.3)
Year 2010 (n = 320)	39 (12.2)	4 (1.3)	277 (86.5)

AdV: Adenovirus; RV: Rotavirus.

antibodies directed against RV and AdV (test lines).

**Statistical analysis**

Data analysis and description of seasonal frequencies were performed using computer software IBM® SPSS® (Statistical Package for Social Sciences) Statistics version 20.0 for Mac. The frequencies of infection were compared into different age and gender groups by  $\chi^2$  test.

**RESULTS**

In total, 509 stool samples were tested and it was possible to detect 63 (12.4%) positive samples for AdV and 4 (0.8%) positive samples for RV (Table 1). Comparing the number of cases during the period between January 2009 and December 2010, it was possible to observe a substantial increase in 2010, however the infection rates were similar.

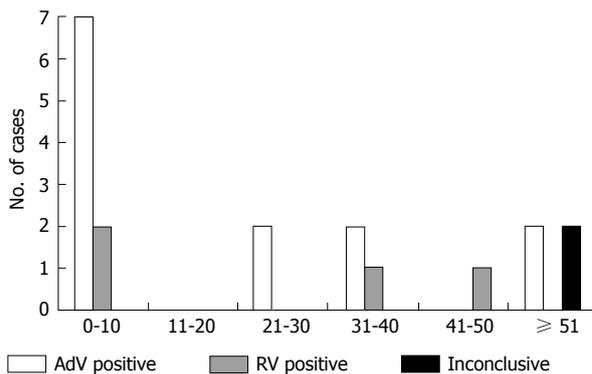
Considering only patients-related data, where we have combined the results of all samples obtained from each individual, the overall frequency of AdV and RV infection was 6.5% (13/200 patients) and 1.5% (3/200 patients), respectively. The prevalence of infection was characterized with stratification of individuals according to age groups and genre and the results showed a tendency to an increased prevalence of infection in paediatric patients between 0-10 years old (Figure 1 and Table 2).

Considering the seasonal distribution of these infections (Figure 2), our study revealed that AdV infection was more frequent between October 2009 and April 2010, while RV infection was characterized by two distinct peaks (April 2010 and July 2010).

**DISCUSSION**

Immunosuppression treatments lead patients to be more susceptible to opportunistic infections, either bacterial or viral. Many studies have shown that RV and AdV are the most frequent pathogenic virus during acute diarrhoea in immunocompromised patients<sup>[3,7,9,13]</sup>. The overall distribution worldwide has been described in literature<sup>[5,14]</sup>, although little is known about the epidemiology of these viruses in Portugal, and therefore we aimed to add epidemiological information of the prevalence of these infections in immunocompromised patients with haematological diseases treated at IPO Porto.

Firstly, it is important to refer that our results should



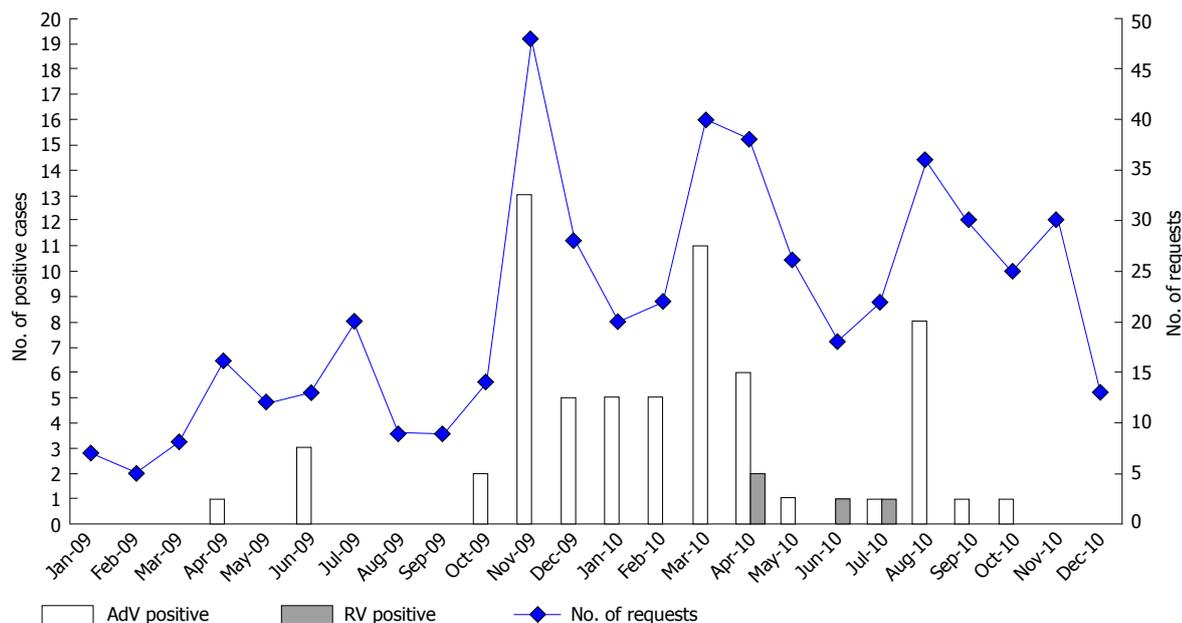
**Figure 1 Age-associated distribution of adenovirus and rotavirus prevalence.** AdV: Adenovirus; RV: Rotavirus.

be discussed considering the limitations of the diagnostic test. This test is used to screen only infections by RV and enteric AdV, which could limit the identification of positive cases since the range of viruses involved in acute gastroenteritis is larger. Nevertheless, the frequencies that we have obtained were considerably low when compared with the number samples. These results might be explained by the fact that other virus such as Norovirus, or even bacteria, could be the cause of the acute gastroenteritis<sup>[15-18]</sup>. Moreover, acute diarrhoea is sometimes overestimated since chemotherapeutic agents and radiotherapy may also promote it<sup>[19]</sup>. In addition, there are no reports of these viruses in Portuguese immunocompromised patients, thus the fact that results are distinct from other studies remain to be further clarified<sup>[20]</sup>.

Recent data indicate that enteric AdV infection in immunocompromised patients remains constant along the year<sup>[3,8]</sup>, and the RV infection is more prevalent during the winter and beginning of the spring<sup>[2-4]</sup>. These features were not observed in our population, and in fact, our study showed that enteric AdV was more prevalent between November 2009 and April 2010, with a seasonal peak in August 2010. Between November 2010 and December 2010 there were no positive cases, but the number of suspected samples was also lower than in the same period the year before.

In contrast with literature, RV incidence was very low, with only four positive cases to be identified, and therefore no seasonal prevalence was estimated<sup>[2,3]</sup>. However, it is possible to observe that positive cases were identified in April and June/July months. These data are in agreement with previous studies performed in Portugal, which describe a higher prevalence of RV infection in paediatric population<sup>[21,22]</sup>. Rodrigues *et al.*<sup>[22]</sup> refers that the prevalence of RV presents clear differences between years and that in 2010 there were two distinct peaks with significant RV activity occurring much later and lasting into July.

To the best of our knowledge, this is the first study to characterize the prevalence of RV and enteric AdV in immunocompromised patients from Portugal. Despite the lower incidence of both viral infections, this study



**Figure 2** Seasonal distribution of adenovirus and rotavirus infection throughout the study period, taking into account the number of requests. AdV: Adenovirus; RV: Rotavirus.

**Table 2** Characterization adenovirus and rotavirus infection by age group and genre *n* (%)

	AdV			RV		
	Positive	Negative	IC	Positive	Negative	IC
Total ( <i>n</i> = 200)	13 (6.5)	185 (92.5)	2 (1.0)	3 (1.5)	196 (98.0)	1 (0.5)
Age group						
0-10 ( <i>n</i> = 60)	7 (11.7)	53 (88.3)	-	2 (3.3)	58 (96.7)	-
11-20 ( <i>n</i> = 21)	-	21 (100.0)	-	-	21 (100.0)	-
21-30 ( <i>n</i> = 19)	2 (10.5)	17 (89.5)	-	-	19 (100.0)	-
31-40 ( <i>n</i> = 19)	2 (10.5)	17 (89.5)	-	1 (5.3)	18 (94.7)	-
41-50 ( <i>n</i> = 19)	-	18 (94.7)	1 (5.3)	-	19 (100.0)	-
≥ 51 ( <i>n</i> = 62)	2 (3.2)	59 (95.2)	1 (1.6)	-	61 (98.4)	1 (1.6)
Genre						
Male ( <i>n</i> = 117)	9 (7.7)	107 (91.4)	1 (0.9)	1 (0.9)	115 (98.2)	1 (0.9)
Female ( <i>n</i> = 83)	4 (4.8)	78 (94.0)	1 (1.2)	2 (2.4)	81 (97.6)	-

AdV: Adenovirus; RV: Rotavirus; IC: Inconclusive.

emphasizes the importance of vigilance and prevention of viral infections in the gastrointestinal tract. Moreover, as the results reveal a lower incidence of RV and enteric AdV, it is extremely important to add more screening methods for other emergent enteric viruses, in order to avoid the morbidity and mortality of the immunocompromised patients.

## ACKNOWLEDGMENTS

Authors are grateful to the Portuguese League Against Cancer (Liga Portuguesa Contra o Cancro - Núcleo Regional do Norte) for the grant of the first author.

## COMMENTS

### Background

Acute gastroenteritis is one of the main causes of morbidity and mortality in

the world, especially for immunocompromised patients. Immunosuppression treatments lead patients to be more susceptible to opportunistic infections, either bacterial or viral. Many studies have shown that rotavirus (RV) and adenovirus (AdV) are the most frequent pathogenic virus during acute diarrhoea in immunocompromised patients.

### Research frontiers

Characterization of RV and AdV prevalence and seasonal distribution in immunocompromised patients with acute gastroenteritis.

### Innovations and breakthroughs

The overall prevalence of AdV and RV infection in immunocompromised patients with acute gastroenteritis was 8%. AdV was the most prevalent with 6.5% (13/200 patients) followed by RV with a prevalence of 1.5% (3/200 patients). Results revealed a lower prevalence of RV and enteric AdV than expected.

### Applications

The lower incidence of RV and enteric AdV observed in the authors' study pointed that it is extremely important to add more screening methods for other

emergent enteric viruses, in order to avoid the morbidity and mortality of the immunocompromised patients.

### Terminology

This study provides the first update on the prevalence of RV and AdV infection as agents of acute gastroenteritis in immunocompromised patients.

### Peer-review

This is an interesting study on the cause of diarrhea by viral agents. The study is well-designed and the manuscript is well-written.

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P- Reviewer: Kamal SA, Mattner J S- Editor: Tian YL

L- Editor: A E- Editor: Liu SQ





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