

## ORIGINAL PAPER

# Rotavirus and adenovirus infections and co-infections as a cause of acute gastroenteritis in hospitalized children – a single centre study

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## ABSTRACT

**Introduction:** Acute infectious diarrhoea or acute gastroenteritis (AGE) is a common gastrointestinal infection that affects children around the world. Viruses are the major pathogens of community-acquired AGE in children. The aim of the study was to establish the main aetiological agents of acute viral gastroenteritis.

**Material and methods:** The study included 1411 patients (aged 1 month to 5 years) hospitalized due to AGE in the Department of Gastrology, Upper Silesian Children's Health Centre, Katowice in the years 2017–2019. All patients' stool samples were screened for the presence of rotavirus and adenovirus antigens by the ELISA method.

**Results:** Aetiological agents were detected in 876 cases (62%). Viral infection was confirmed in 286 cases (56%). In this group of patients, 239 (59%) children had confirmed rotavirus (RV) aetiology, 28 (13%) had adenovirus (AV), and 19 (12%) had simultaneous RV and AV infection. There was a decrease in the number of hospitalizations due to AGE of RV aetiology (in 2017 – 83.5%, 2018 – 33%, in 2019 – 35%,  $p < 0.05$ ). In the same period, there was a significant increase in the number of AV infections: from 9.8% in 2017 to 35% in 2018 and 39% in 2019 ( $p < 0.05$ ). The increasing frequency of RV and AV co-infections is also noteworthy, from 6.7% children in 2017 to 30.9% and 25% patients respectively in 2018 and 2019 ( $p < 0.05$ ). Early spring and late winter seasonality was observed only in the case of RV. No seasonality of adenoviral infections was found.

**Conclusions:** Rotavirus infections are the leading cause of hospitalization of children in spring and late winter months, whereas adenoviruses showed no clear seasonality.

## KEY WORDS:

children, adenovirus, acute gastroenteritis, rotavirus.

## INTRODUCTION

Acute infectious diarrhoea, or acute gastroenteritis (AGE), is a common gastrointestinal infection that affects children around the world [1]. According to the Federation of International Societies of Pediatric Gastroenterology, Hepatology, and the Nutrition Working Group, AGE is characterized by the presence of diarrhoea defined as a decrease in the consistency of stool leading to loose or

liquid stools and/or an increase in the frequency of evacuations to three or more in 24 hours, with or without fever or vomiting [2].

Viruses are the major pathogens of community-acquired AGE in children. Rotavirus is the most common cause of AGE in children in all European countries [1, 3]. Rotavirus is also the leading aetiology for diarrhoea mortality among all children younger than 5 years at the global level [3]. In Poland, according to the data of the Polish

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Institute of Hygiene 34,019 people had viral AGE in 2019. Rotavirus was the most common cause of acute diarrhoea, regardless of age group; the highest morbidity was in children under 5 years old (1400/100,000) [4].

In 2016, diarrhoea was the eighth leading cause of mortality, responsible for more than 1,6 million deaths and the fifth leading cause of death among children younger than 5 years [1, 3]. Most diarrhoeal deaths occurred among children younger than 5 years, and occurred in south Asia and sub-Saharan Africa. The diarrhoea mortality rate in children under 5 years old in Poland is low ( $< 1/100,000$  deaths) [3, 4]. The major concerns involve the risk of complications, essentially dehydration and malnutrition, especially in vulnerable patients: young children, the elderly, and patients with immunosuppression.

In recent years much progress has been made in the reduction of diarrhoea burden among children younger than 5 years; however, diarrhoea remains a leading cause of death and morbidity [1].

The aim of the study was to establish the main aetiological agents of acute viral gastroenteritis.

## MATERIAL AND METHODS

The study was conducted at the Department of Gastroenterology, Upper Silesian Children's Health Centre, Katowice in the years 2017–2019. 1411 medical records of children aged 1 month to 5 years hospitalized due to AGE were subject to retrospective analysis.

All patients' stool samples were screened for the presence of rotavirus and adenovirus antigens by the ELISA method (Hangzhou All Test Biotech Co, China). Depending on the clinical course, stool cultures for *Salmonella*, *Shigella*, pathogenic *E. coli*, and *Campylobacter pylori* were performed. Faecal samples were obtained during 48 hours of hospitalisation. Statistical analysis was conducted using the procedures available in licenced Statistica software (StatSoft, Poland, 2020).

## RESULTS

A total of 1411 stool samples were examined, and aetiological agents were detected in 876 cases (62%). The incidence of viral AGE did not change over the observed years ( $p = 0.17$ ), in contrast to bacterial infections, the number of which decreased in the following years ( $p = 0.01$ ) (Table 1).

In 2017, 512 children with AGE were hospitalized at the Department of Gastroenterology. Viral infection was confirmed in 56% of cases. In this group of patients, 83.5% of children had confirmed rotavirus (RV) aetiology, 9.3% had adenovirus (AV), and 6.7% had simultaneous RV and AV infection.

In the following years, there was a decrease in the number of hospitalizations due to AGE of RV aetiology

TABLE 1. Annual aetiology of acute gastroenteritis

Parameters	2017 n (%)	2018 n (%)	2019 n (%)	p-value
Aetiology				
Viral	286 (56)	237 (51)	243 (56)	0.17
Bacterial	50 (10)	40 (9)	20 (5)	0.01
Unknown	176 (34)	190 (40)	169 (39)	0.1
Total	512	467	432	

TABLE 2. Frequency of rotaviruses, adenovirus and rotaviruses-co-infection in 2017–2019

Year	Aetiology		
	RV n (%)	AV n (%)	RV + AV n (%)
2017	239 (83.5)	28 (9.8)	19 (6.7)
2018	79 (33.5)	85 (35.8)	73 (30.9)
2019	87 (35.8)	95 (39.1)	61 (25.1)

AV – adenovirus, RV – rotavirus

(in 2017 – 83.5%, 2018 – 33%, in 2019 – 35% of all viral infections,  $p < 0.05$ ). However, in the same period, there was a significant increase in the number of AV infections: from 9.8% in 2017 to 35% in 2018 and 39% in 2019 ( $p < 0.05$ ). The increasing frequency of simultaneous RV and AV infections is also noteworthy, from 6.7% children in 2017 to 30.9% and 25% patients respectively in 2018 and 2019 ( $p < 0.05$ ) (Table 2).

Early spring and late winter seasonality was observed only in the case of RV and it was similar in the studied years ( $p < 0.05$ ) (Figure 1).

There was no correlation between AV incidence and the season of the year. The highest morbidity in AV infection was different in observed years, in 2017 from May to September, in 2018 from September to December, and in 2019 the highest incidence of AV infection was recorded in February and from October to December ( $p > 0.05$ ) (Figure 2).

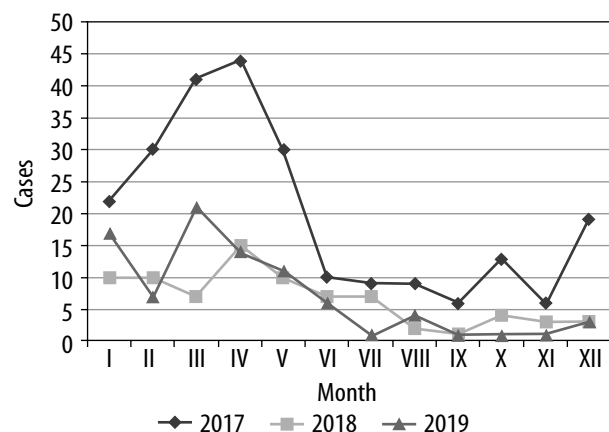


FIGURE 1. Monthly distribution of rotavirus infections

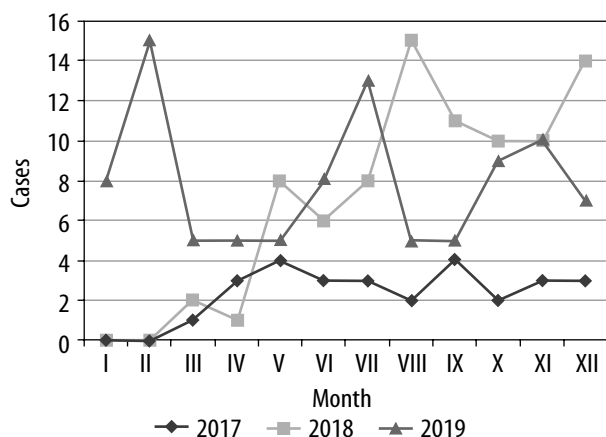


FIGURE 2. Monthly distribution of adenovirus infections

## DISCUSSION

In our study more than half of the children hospitalized due to AGE suffered from viral infection, which corresponds with the current knowledge. It is estimated that 60–75% of cases of patients hospitalized with AGE are caused by viruses [1, 4, 5]. Most of these infections were caused by RV, but their incidence declined over the observed years. However, in the same period, there was a significant increase in the number of AV infections (from 9.8% in 2017 to 39% in 2019 patients with viral AGE). These data are consistent with other papers. The REVEAL study showed that RV gastroenteritis in children under 5 years old is responsible for 53–68% of cases of viral AGE admitted to hospitals [6]. In a Polish study conducted in 2014 33% of children hospitalized with AGE had RV infection [7]. Based on available literature on the RV burden in Western Europe the incidence rates for RV AGE in the under 5 y.o. population ranged between 1.33 and 4.96 cases per 100 person-years. However, the incidence rate of RV AGE is likely underestimated as many patients receive care at home [8].

On the other hand, there was a significant decrease in the number of hospitalizations due to AGE of RV aetiology (from 83% in 2017 to 35% in 2019,  $p < 0.05$ ), which may be a result of widespread RV immunization. Prevention of rotavirus infection through vaccination appears to be the only effective option because RV AGE shows a similar incidence in children throughout the world regardless of hygiene and development standards [9, 10]. The level of vaccination of infants against RV is increasing despite the fact that until now vaccination in Poland was financed entirely by parents. During the analysed period in the Silesian Voivodeship 10,320 children were vaccinated in 2017, 11,181 in 2018, and in 2019 11,807 children [11–13]. A further decline in the number of cases is expected in the next years due to the introduction of compulsory vaccination against RV in 2021. On the other hand, a Polish study conducted in 2016 found that 4.7% of children hospitalized with rotavirus diarrhoea had previously been vaccinated against this infection; no severe

cases were seen [7]. It is estimated that introduction and expanded use of the rotavirus vaccine was responsible for a 2.6% decrease in mortality of children younger than 5 years due to diarrhoea between 2000 and 2016, and its use prevented nearly 27000 deaths in 2016 [1].

In recent literature it was stated that adenoviruses were responsible for 5–15% of gastroenteritis cases in infants and pre-school children; the clinical course was milder in children whose immune systems were sufficient [14]. The conducted study showed an increase in the incidence of AV gastroenteritis (from 9.8% patients in 2017 to 39% in 2019), which is more than data from the literature [10, 15].

In the past, AGE was generally attributed to a single causative agent known to be associated with clinical symptoms. However, due to their high prevalence, exposure to multiple viruses at similar times can potentially occur in the same host, and these viruses may infect simultaneously [16]. There are limited data available on co-infections in AGE cases, and the rate of such infections differ widely in the literature. In a study from Spain on children with AGE viral co-infections were detected in 21% of cases [5]. In Turkish children under the age of 5, co-infections were found in 10.4% of samples (mostly RV and norovirus, and norovirus and AV) [17]. A long-term study (11 years) in Italy showed the incidence of co-infection at 8.3%; the most common viral combination was rotavirus with norovirus (70.6% of co-infections) or with astrovirus (9.6%) [18].

Rotavirus seasonality has been shown to differ widely across the world. Rotavirus was common in colder/winter months. Relationships between monthly rotavirus incidence and climatological variables, such as temperature, rainfall, and relative humidity, suggest that rotavirus infections tend to increase under cool and dry conditions in temperate climates [15, 19]. In the present study viral diarrhoea caused by RV mostly occurred in the autumn–winter months. In contrast to RV infection, the prevalence of AGE caused by AV showed no clear seasonality but the seasonal difference could not be assessed because of the low case number. This is consistent with previous reports [15]. Most AV epidemics occur in the winter or early spring, but infections occur throughout the year with no clear seasonality [19].

Our study was conducted on a large number of hospitalized children, which is its strength as well as the long duration. The clinical course of AGE was typical of viral infections and was not analysed. We generated valuable information on the incidence of RV and AV gastroenteritis and on the magnitude of mixed viral infections in a large study population hospitalized with AGE. So far, there has been no information about viral co-infections among children hospitalized due to AGE in Poland. On the other hand, the weakness of this study was that the number of patients vaccinated against RV has not been estimated. Another limitation of our study was the limited number of viruses we identified, particularly

the lack of diagnosis of norovirus and astrovirus infections, which are increasingly often diagnosed.

## CONCLUSIONS

Rotavirus infections are the leading cause of children's hospitalization in spring and late winter months whereas adenoviruses showed no clear seasonality.

There is a great need to apply molecular diagnostic tools to determine the wider spectrum of viral aetiology and monitor the changing aetiology of acute enteritis in the Polish population.

## DISCLOSURE

The authors declare no conflict of interest.

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