

# CLINICAL MANIFESTATIONS IN ROTAVIRUS VERSUS NOROVIRUS INFECTIONS – OBSERVATIONS BASED ON 124 CASES OF VIRAL DIARRHEA IN CHILDREN

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## Abstract

**Background:** Viral diarrhea is caused in children mainly by the rotavirus and norovirus. The aim of this study is to detect specific clinical elements to rapidly distinguish between the two types of digestive infections. **Methods:** This study has been prospectively elaborated by selecting two viral groups of rotavirus and norovirus respectively that have been confirmed by the Elisa Ridascreen test. Clinical parameters have been followed by filling a questionnaire by parents and a personalised medical record by the medical doctor treating the patient. Statistical processing of the obtained data has been performed using Student's t-test and the „Z-test” employing the Stata v12 statistical software. **Results:** For statistical processing of the data, the threshold value for the significance level (p) was set at 5%, (standard  $\alpha = 0.05$  cutoff). The first symptom was for the rotavirus infection: vomiting (35.5%), diarrhea (35.5%) and fever (23.7%), compared to diarrhea (38.7%), fever (35.5%) and vomiting (25.8%) for the norovirus infection, the differences being statistically negligible ( $p > 0.05$ ). The fever in the first day was percentually lower in rotavirus infection in the 38.1-39°C interval but higher in the norovirus infection between 39.1 - 40°C (with no statistical significance). The norovirus infection shows persistent fever until day 5 whereas rotavirus infection remains until day 4. Vomiting precedes diarrhea in most of the cases ( $p > 0.05$ ). Stools with bloody streaks are present mainly in the rotavirus infection (10.8% to 3.2%,  $p > 0.05$ ). In day 5 a higher number of cases show persistent diarrhea in the case of norovirus infection compared to rotavirus infection. The only statistically significant data were for rhinorrhea ( $p < 0.05$ ), the rest of the neurological symptoms, coughs, myalgias being statistically negligible. **Conclusions:** The only difference statistically significant is rhinorrhea that is present most frequently in norovirus infections compared to rotavirus infections ( $p < 0.05$ ).

**Key words:** diarrhea, rotavirus, norovirus, clinical picture, child.

## Introduction

Infectious diarrhea remains the main morbidity and mortality cause among children under five years (1). The

rotavirus holds the chief position among the main pathogens that also include the norovirus, enteropathogenic and enterotoxigenic Escherichia coli, type 40/41 adenovirus, astrovirus and sapovirus. It was estimated that rotaviruses are responsible for about 453.000 deaths annually mainly in countries from Africa and Asia (2). The noroviruses are the second main cause for viral gastroenteritis in children under five and are estimated to cause about 200.000 deaths annually among the children from this age group in the developing countries (3).

Beside classic viruses, some new picornaviruses (Aichi virus, parechovirus, enterovirus) considered to be associated with the diarrhea in humans, have been identified in parallel with the evolution of molecular diagnostic methods (4).

The rotaviruses are transmitted by the oral-fecal route and are extremely contagious. This facilitates viral transmission especially in day care centres and hospitals. The rotavirus infection is the cause of acute gastroenteritis with diarrhea and different stages of dehydration. This results mainly from the destruction of the erythrocytes from the intestinal villi, affecting the ion transport and absorption. The highest incidence of rotavirus infection is during winter and summer in the countries with temperate climate. Many children have an asymptomatic infection that maintains the circulation of the rotavirus in the population (5).

The acute gastro-intestinal infections and diarrhea with vomiting are frequently encountered in ambulatory care. Due to a mainly auto limiting evolution, establishing the diagnosis is often useless. The viral infections caused by the noro- or rotaviruses are the most frequent infections. Bacterial infections are less frequent due to higher hygiene standards in the developed countries. In hospitals and after antibiotic treatments, Clostridium difficile is the main cause of diarrhea (6).

After an significant decrease in acute gastroenteritis caused by the rotavirus in children, due to the introduction of two vaccines (7), the norovirus has become the main cause of such disease in children below five in the US (8).

The incidence of viral diarrhea in Romania is unknown. The actual studies show limited groups for small geographical areas - București (9, 10), Cîsnădie (11). The majority of these studies are related to the rotavirus.

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Studies concerning the norovirus have not been reported in Romania. Although, there are a few studies on clinically predictive factors in viral diarrhea (12, 13, 14), there are no studies regarding scoring systems for the viral etiology.

In the literature, there are only two scoring scales used to establish the severity of the viral diarrhea: the modified Vesikari score (15) and the Clark score (16). However, these two scores cannot be used to predict the viral etiology of diarrhea (17,18, 19).

Both the rotavirus and norovirus infections are viral diseases of the digestive system with great impact upon the health of a child. The manifestations are considered more severe in rotavirus infections, affecting the younger age and are less severe in norovirus infection. Therefore, a rapid clinical differentiation between the two would be useful for the approach and monitoring method.

The aim of this study is to differentiate between the clinical elements in rota- and norovirus infections in children.

**Material and method:**

A prospective longitudinal study was performed between October 2014 and January 2016 within the P1/4 internal UVVG grant frame.

The study was performed on children with diarrhea hospitalized in the pediatric ward that screened positively for norovirus/rotavirus using the RIDA SCREEN test. These children were divided in two groups: ROTAVIRUS and NOROVIRUS respectively.

Group 1: ROTAVIRUS was made up of 93 children of which 46.2% were girls and 53.8% boys. The median age was 4.54 (0 – 17 years).

Group 2: NOROVIRUS was made up of 31 children of which 32.9% were girls and 67.7% boys. The median age was 3.71.

The information from the questionnaire and personalized medical record corresponding to each child

from the viral sub-group were introduced in an Excel database. The following parameters were monitored: first symptom, the fever in the first day, the fever during the first 5 days, the duration of the fever, number of the vomitings and stools during 5 days, duration of stools, the vomiting-stool chronology, aspect of the stools, duration of the diarrheic stools, presence of other symptoms: agitation, sleepiness, nasal secretions, myalgias, shivers and coughs.

The statistical processing of the collected data was done with the Stata v12 statistical software using Student's t-test and the „Z-test” to identify clinical parameters that are statistically significant to differentiate between the two groups.

Note: the study was approved by the Ethics Committee of UVVG Arad and the parents signed an agreement for this study.

**Results**

In this work, to determine the clinical parameters that are statistically significant to differentiate between the two groups under study, the threshold value for the significance level (p) was set at 5%, (standard  $\alpha = 0.05$  cutoff).

Table 1 shows the gender and age distribution of the two groups. The median for females with norovirus is four years (1 year minimum and 16 maximum) and for rotavirus is 2.5 years (1 year minimum and 15 maximum). The median for males with rotavirus is 5 years (minimum 0 years and 17 maximum) and for norovirus is 2 years (minimum 0 years and 12 maximum). There is no significant difference between the median ages of the two groups ( $p>0,05$ ).

Table 2 shows the distribution of the first symptom in the two groups under study. A higher frequency of the fever and vomiting can be observed in the rotavirus group compared with the norovirus group but without statistical significance.

Table1. Gender and age distribution of the groups.

		ROTAVIRUS							NOROVIRUS						
		#	%	Mean	Median	SD	Min	Max	#	%	Mean	Median	SD	Min	Max
Sex	F	43	46						10	32					
	M	50	54						21	68					
Age (years)	F	43		4.72	4	3.5	1	16	10		4.1	2.5	4.5	1	15
	M	50		4.36	5	3.3	0	17	21		3.33	2	3.4	0	12

Table 2. The distribution of the first symptom in the two groups.

	ROTAVIRUS	NOROVIRUS	z-value	p-value
Fever	22 (23.7%)	11 (35.5%)	1.29052	0.19687
Diarrhea	33 (35.5%)	12 (38.7%)	-0.32348	0.74633
Abdominal colic	3 (3.2%)	0	-1.01232	0.31138
Vomiting	33 (35.5%)	8 (25.8%)	0.99189	0.32125

Coughs	2 (2.2%)	0		
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There were no significant differences regarding the febrile curve from the first 5 days or the intensity of the fever from day one (Figures 1 and 2).

The average duration of the vomiting is  $1.7 \pm 1.39$  days for ROTAVIRUS group and  $1.35 \pm 1.45$  days for NOROVIRUS group respectively. There is no significant difference in the duration between the two groups ( $p > 0.05$ ). (Figure 3)

The aspect of the stool was watery in 88.2% vs. 90.3% rotavirus/norovirus, mucus in 6.5% norovirus and with bloody streaks in 10.8% vs. 3.2% rotavirus/norovirus. Although percentually the rotavirus infection is characterised predominantly by invasive stools compared with norovirus infection, the difference is not significant statistically (Figure 4).

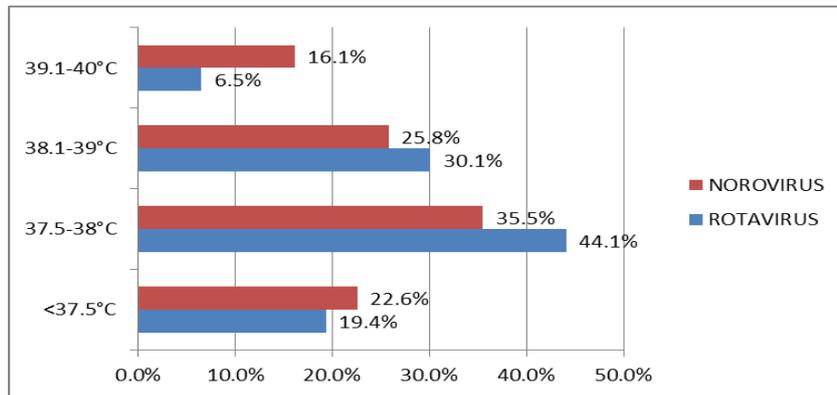


Figure 1. Fever in the first day.

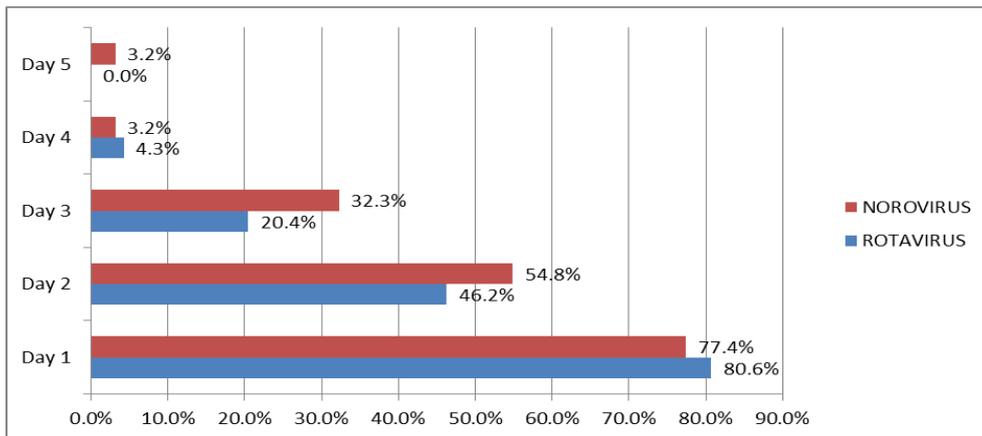


Figure 2. Fever during five days.

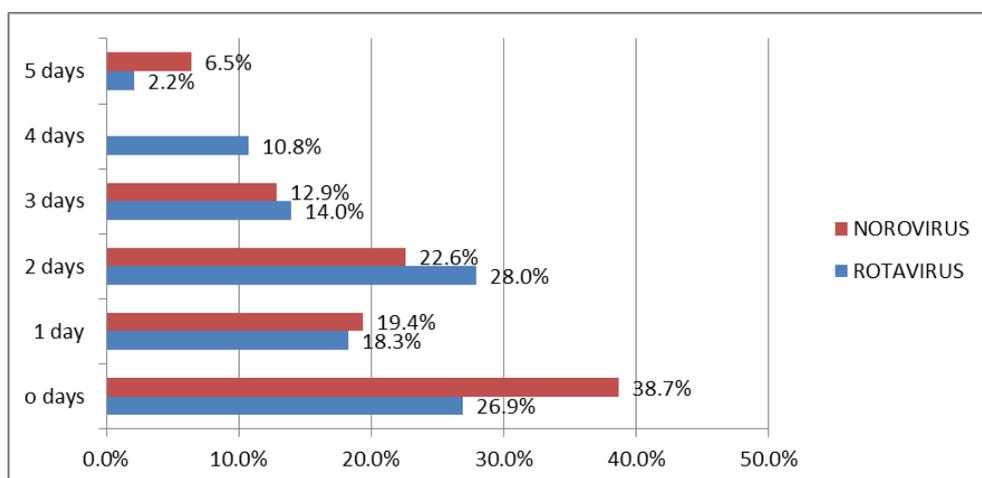


Figure 3. Duration of vomiting.

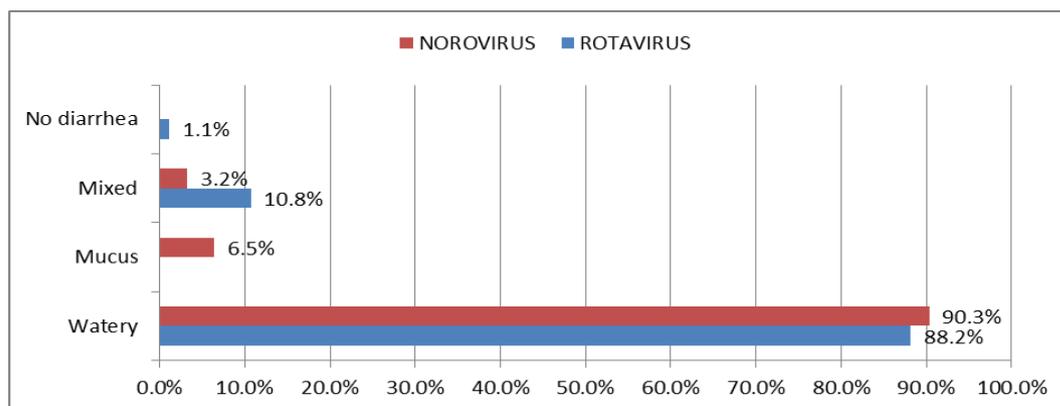


Figure 4. The aspect of stools.

The number of stools was  $4.39 \pm 2.20$  for ROTAVIRUS group and  $3.93 \pm 1.74$  for NOROVIRUS group respectively.

In the fifth day a higher number of cases of norovirus infection showed persistent diarrhea compared to rotavirus infection, without statistical significance for the two groups. (Figure 5)

Table 3 shows the associated symptoms present in the norovirus and rotavirus infections. It can be observed that among the associated clinical symptoms, only the rhinorrhea linked with the norovirus infection has a statistical significance.

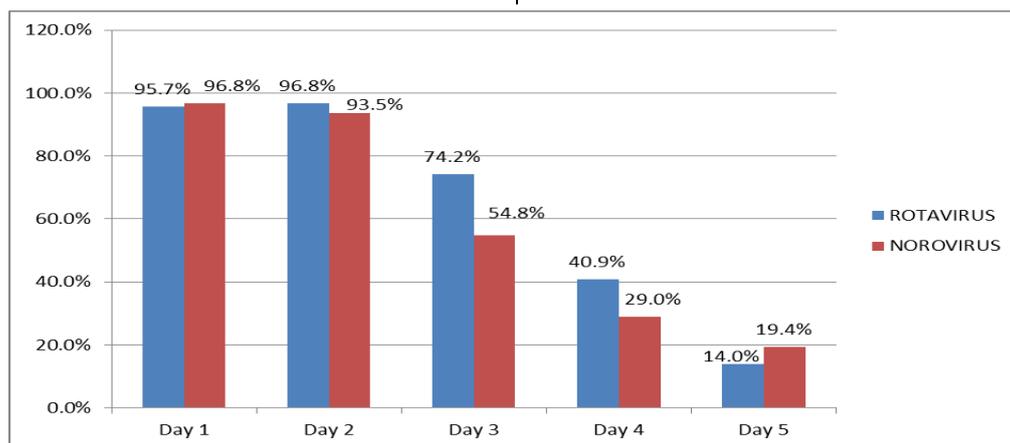


Figure 5. Persistence of diarrheic stools.

Table 3. Associated symptoms.

Associated symptoms	LOT		p-val
	Rotavirus	Norovirus	
Coughs	15	10	0.05257
	16.10%	32.30%	
Myalgias	16	1	0.05004
	17.20%	3.20%	
Nasal secretions	12	10	0.01457
	12.90%	32.30%	
Shivers	7	0	0.11582
	7.50%	0	
Convulsions	4	1	0.79211
	4.30%	3.20%	
Sleepiness	28	9	0.90978
	30.10%	29.00%	
Agitation	30	16	0.05337
	32.30%	51.60%	

TOTAL	93	31	
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### Discussions

Rotavirus and norovirus infections are the most frequent causes for the viral diarrhea in children.

The first symptom was for the rotavirus infection: vomiting (35,5%), diarrhea (35,5%) and fever (23,7%), compared to diarrhea (38,7%), fever (35,5%) and vomiting (25,8%) for the norovirus infection, the differences being statistically negligible ( $p>0,05$ ).

The fever in the first day was percentually lower in rotavirus infection in the 38,1-39°C, interval but higher in the norovirus infection in the 39,1-40°C (with no statistical significance).

The norovirus infection shows persistent fever until day 5 whereas rotavirus infection remains until day 4.

Vomiting precedes diarrhea in most of the cases, having no statistical significance ( $p>0,05$ ). Stools with bloody streaks are present mainly in the rotavirus infection (10,8% to 3,2%) again without statistical significance ( $p>0,05$ ).

In day 5 a higher number of cases show persistent diarrhea in the case of norovirus infection compared to rotavirus infection.

The only statistically significant data were for rhinorrhea ( $p<0,05$ ), the rest of the neurological symptoms, coughs, myalgias being statistically negligible.

O’Ryan (20), following a comparative study of rotavirus vs. norovirus showed that the rotavirus infection has a higher severity score than norovirus infection with a higher number of stools and more frequent fever. The duration of diarrhea, the shivers and intensity of vomiting was identical for the two groups. The severity of viral BDA in infants was the same.

It was noticed that the number of BDA with norovirus infection is on the rise, same as the moderate/severe forms which requires the use of a vaccine.

Narkeviciute (21), on a group comprised of 50 children with BDA with norovirus infection and 50 children with rotavirus infection, noticed that the rotavirus infection shows more frequently fever and diarrhea and in norovirus infection the vomiting is more frequent.

O’Ryan (22) highlights that each child shows an average of 1.4 BDA until 18 months of which 15% are rotavirus infections and 18% are norovirus infections. Rotavirus infection was more severe than the norovirus

infection independent of vomiting. The re-infections with the norovirus are more frequent than with the rotavirus.

Abugalia (23) on 164/91 rotavirus/norovirus noticed that the rotavirus was identified in the hospitalised patients and the norovirus in those from ambulatory care.

Doll (24), following a study, believes that the patients with rotavirus show more often fever, intense dehydration, a higher number of stools and those with norovirus have higher number of vomitings within 24 hrs compared to non-specific gastroenteritis.

Our study suggests that the number of vomitings is percentually higher in norovirus infection than in rotavirus infection but it doesn’t have any statistical significance ( $p>0,05$ ).

From the above, it can be observed the wide range of parameters followed by various authors in different associations without being able to achieve a net clinical differentiation of the etiology for the two types of groups.

### Conclusions

1. The duration of the fever and stools was percentually longer in the norovirus infection vs. rotavirus infection

2. The norovirus infection is associated with a higher number of vomitings in the first day but of a shorter duration compared to rotavirus infection

3. The stools with bloody streaks are mainly present in rotavirus infection, without statistical significance

4. Rhinorrhea is present more frequently in norovirus infections compared to rotavirus infections, the differences being statistically significant ( $p<0,05$ ).

5. Despite the many clinical parameters studied, only rhinorrhea is statistically significant in the differential diagnostic norovirus vs. rotavirus infection for the group under study.

### Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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