

CLINICAL ASPECTS OF ROTAVIRUS DISEASE IN CHILDREN FROM SOUTH-EAST OF ROMANIA

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ABSTRACT

Background. Gastroenteritis with rotavirus is the leading cause of severe diarrhea among infants and young children.

The aim of the study was to evaluate the clinical aspects of the rotavirus gastroenteritis comparatively with non-rotavirus disease.

Material and methods. We conducted an observational, retrospective study, that included children hospitalized in the Clinical Hospital of Infectious Diseases from Constanța, Romania, between 2011-2012. We analyzed the medical records of the patients and extracted demographic data, temperature, frequency of vomiting and diarrheic stools, degree of dehydration, duration of parenteral rehydration and hospitalization. We compared two groups of children: 505 with rotavirus disease and 100 with non-rotavirus disease.

Results. There were statistically significant differences ($p=0.001$) between the mean age of the two groups, the number of days of hospitalization, the maximum number of stools per day, the maximum number of vomiting per day. There were no statistically significant differences between the two groups regarding the maximum temperature value ($p=0.96$).

RÉSUMÉ

Aspects cliniques de la maladie à rotavirus chez les enfants

Introduction. La gastro-entérite à rotavirus est la principale cause de diarrhée sévère chez les nourrissons et les jeunes enfants.

Objectifs. Nous avons essayé à évaluer les aspects cliniques de la maladie rotavirale par rapport à la gastro-entérite non rotavirale.

Méthodes. Nous avons effectué une étude d'observation, rétrospective qui comprenait des enfants hospitalisés à l'hôpital clinique de maladies infectieuses de Constanța, entre 2011-2012. Nous avons analysé les dossiers médicaux des patients en insistant sur les données démographiques, la température, la fréquence des vomissements et des selles diarrhéiques, le degré de déshydratation, la durée de réhydratation par voie parentérale et l'hospitalisation. Nous avons comparé deux groupes d'enfants: 505 avec la maladie rotavirale et 100 avec une maladie non rotavirale.

Résultats. Il y avait des différences statistiquement significatives ($p=0,001$) entre l'âge moyen pour les deux groupes, le nombre de jours d'hospitalisation, le nombre maximum de selles par jour, le nombre maximum

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Conclusions. Evolution of the rotavirus disease is more severe and prolonged comparatively with non-rotavirus gastroenteritis.

Key words: rotavirus, gastroenteritis, children.

INTRODUCTION

Acute diarrheal diseases have always been a public health problem, accompanying humanity throughout history. Acute diarrheal disease is still an important cause of infantile mortality in the world, annually being reported 5-10 million of deaths.^{1,2} In the past, bacterial digestive infections (cholera, bacillary dysentery, typhoid fever) caused significant epidemics, with important mortality; currently, due to improvement of living conditions, health and well-being, diagnostic possibilities and antibiotic treatment on a large scale, an etiological „turn“ of viral infections has been observed.³ Thus, nowadays, acute viral gastro-intestinal infections have become the major digestive infections in younger age groups (pre-school children).³ Ages most frequently involved are between 3 months and 2 years.^{2,3,4,5} Diarrhea syndrome is favored by many factors and pathogens. Rotavirus infection is of particular interest, being a frequent cause of acute diarrheal disease in young children. All children by age of 5 years presented an acute episode of rotavirus diarrhea.^{3,6} Acute viral gastroenterocolitis is determined mainly by rotaviruses, caliciviruses, adenoviruses and astroviruses.³ There are also other viruses (Coronaviruses and picornaviruses) that can cause diarrheal diseases, but due to diagnostic difficulties in medical practice, their importance remains unclear.³ Nowadays, rotavirus remains the most important etiology of diarrheal disease in infants and small children.^{1,2,3}

THE OBJECTIVES OF OUR STUDY were to observe the peculiarities of rotavirus infection in children admitted to the Infectious Diseases Hospital Constanta, Romania, in the period January 1st, 2011 – December 31st, 2012; to assess the epidemiological aspects of infection with rotavirus; to evaluate the clinical and laboratory aspects of this infection and compare it with clinical and laboratory aspects of acute diarrheal disease with other triggers; to observe the evolutionary aspects of rotavirus infection; to assess the need for vaccination.

MATERIAL AND METHODS

We realized a descriptive, observational, non-interventional, prospective and retrospective study, on

de vomissements par jour. Il n'y avait pas de différences statistiquement significatives entre les deux groupes en ce qui concerne la température maximale ($p=0,96$).

Conclusion. L'évolution de la maladie à rotavirus est plus sévère et prolongée.

Mots clés: rotavirus, la gastro-entérite, enfants.

patients with acute diarrheal disease hospitalized in the pediatric ward of the Infectious Diseases Hospital Constanta, Romania, over a period of two years (2011-2012).

Inclusion criteria:

- Children hospitalized with acute diarrheal disease.
- Diagnosis confirmed by a positive test for determining rotavirus by latex agglutination in faeces.

Statistical analysis:

The experimental data were processed using the IBM SPSS Statistics 20 Statistical Processing Program. The procedures used were: descriptive statistics (for the characterization of discrete and continuous variables defined at the database level); charts; non-parametric statistical tests (the χ^2 association test, the relationship between two categorical variables, with the determination of the risk / OR chance and relative risk Rr); parametric statistical tests (Independent Samples tTest). A $p < \alpha = 0.05$ was considered statistically significant.

Parents' informed consent and Ethic Committee's agreement of Clinical Infectious Diseases Hospital were obtained for this study.

RESULTS

The general characteristics of both groups, Rotavirus (+) and Rotavirus (-), are presented in Table 1 and Table 2.

The general characteristics of patients with rotavirus disease are presented in Table 1: mean age 2.54 years, majority were boys (53.9%), from urban area (72.3%), hospitalised between March and May (40.8%), with first degree of dehydration (69.7%). The most affected group of age in the rotavirus group was 1-2 years, which represents 45.3% from the total patients with rotavirus gastroenteritis. Nosocomial infections with rotavirus were registered in 19.4% of the cases. Respiratory diseases were the most frequent diseases (31.7%) associated with rotavirus gastroenterocolitis. The average number of days of hospitalisation in this group was 6.84 days. Regarding symptoms, we found that 95% of children from the study group had fever, 80% of children presented vomiting and 70.3% presented more than 3-6 stools per day.

Table 1. General characteristics of patients with Rotavirus gastroenteritis (Group 1).

Variable	
Age (years), [average, (min-max)]	2.54; (4months, 1years)
0-1year [N, (%)	8; 1.58
1-2 years [N, (%)	229; 45.3
2-3 years [N, (%)	85; 16.83
3-4 years [N, (%)	66; 13.06
4-5 years [N, (%)	49; 9.7
5-11 years [N, (%)	68; 13.47
Sex M [N, (%)	272; 53.9
Sex F [N, (%)	233; 46.1
Urban environment [N, (%)	365; 72.3
Rural environment [N, (%)	140; 27.7
Hospitalization December-February[N, (%)	94; 18.6
Hospitalization March-May[N, (%)	206; 40.8
Hospitalization June-August[N, (%)	128; 25.3
Hospitalization September-December[N, (%)	77; 15.2
Fever-yes [N, (%)	480; 95
Fever-no [N, (%)	25;5
Maximum temperature(Celsius degrees)[average; (min-max)]	37.975; (37.5-39.3)
Stools/day [average; (min-max)]	5.11; 3-10
3-6 stools/day [N, (%)	355; 70.3
>6 stools/day [N, (%)	150; 29.7
Vomiting-yes [N, (%)	404; 80
Vomiting-no [N, (%)	101; 20
Maximum number of vomiting/day	7
<3 vomiting/day [N, (%)	480; 95
4-7 vomiting/day [N, (%)	25;5
Vomiting/day [average]	1.487
Toxicity -yes [N, (%)	149; 29.5
Toxicity -no [N, (%)	356; 70.5
Nosocomial infection-yes [N, (%)	98; 19.4
Nosocomial infection -no [N, (%)	407; 80.6
Degree of dehydration I [N, (%)	352; 69.7
Degree of dehydration II [N, (%)	146; 28.9
Degree of dehydration III [N, (%)	7; 1.4
Days of hospitalization [average; (min-max)]	6.84; (1-21)
Hb(g/dL) [average; (min-max)]	10.73; (6.6-14)
WBC/mm ³ [average; (min-max)]	8640.59; (2400-20700)
Fibrinogen (mg%) [average; (min-max)]	365.86; (260-710)
ESR (mm/h) [average; (min-max)]	11.45; (4-40)
Association with respiratory diseases [N, (%)	160; 31.7
Association with digestive diseases [N, (%)	52; 11
Association with eruptive diseases [N, (%)	11; 2.2

The general characteristics of group 2 (patients with nonrotavirus diseases) are presented in Table 2: mean age 4.34 years, the majority were boys (52%), from urban area (77%), hospitalised between June and August (34%), with first degree of dehydration (71%). The average number of days of hospitalisation in this group was 5.96 days. Fever was present in 86% of cases, vomiting in 40% and 3-5 diarrhetic stools per day in 98% of studied children.

Table 2. General characteristics of patients without Rotavirus infection (Group 2).

Variable	
Age (years)[average; (min-max)]	4.34; (2;11)
Sex M [N; (%)	52; 52
Sex F [N; (%)	48; 48
Urban environment [N; (%)	77; 77
Rural environment [N; (%)	23; 23
Hospitalization December-February [N; (%)	26; 26
Hospitalization March-May [N; (%)	25;25
Hospitalization June-August [N; (%)	37;37
Hospitalization September-December [N; (%)	12;12
Fever-yes [N; (%)	86;86
Fever-no [N; (%)	14;14
Maximum temperature(Celsius degrees) [average; (min-max)]	37.8; (37.5-38.8)
Vomiting-yes [N; (%)	40; 40
Maximum number of vomiting/day	4
<3 vomiting/day [N; (%)	98; 98
4 vomiting/day [N; (%)	2;2
Diarrhetic stools/day [average; (min-max)]	4.2; (3-6)
3-5 Diarrhetic stools/day [N; (%)	98; 98
6 Diarrhetic stools/day [N; (%)	2;2
Toxicity-yes [N; (%)	19; 19
Toxicity -no [N; (%)	81;81
Degree of dehydration I [N; (%)	71;71
Degree of dehydration II [N; (%)	29;29
Days of hospitalization[average; (min-max)]	5.96; (2-15)
Hb (g/dL) [average; (min-max)]	10.56; (7,4-13,7)
WBC/mm ³ [average; (min-max)]	9679; (3100-18300)
Fibrinogen(mg%) [average; (min-max)]	403.41; (212-696)
ESR (mm/h) [average; (min-max)]	15.37; 4-37

When we compared the mean value of inflammatory tests in both groups, we have found that in group 1 – Rotavirus (+) – the mean value of fibrinogen was normal (365.86 mg/dL), and erythrocyte sedimentation rate (ESR) was slightly higher than

normal (11.45 mm/1h), in contrast with group 2, in which mean value of fibrinogen (403.41 mg/dL) and ESR (15.37 mm/1h) were above the normal value.

We noticed that first degree of dehydration was predominant in both groups (69.7% in group 1 and 71% in group 2), but third degree of dehydration was present only in group 1 and absent in group 2.

When comparing the mean age in both groups, we found that in the rotavirus group the mean age was lower than in the nonrotavirus group ($p < 0.001$). The mean age in rotavirus group was 2.54 years, with limits between 4 months and 11 years, and in the nonrotavirus group was 4.34 years, ranging between 2 and 11 years old (Figure 1). Because $p < 0.001 < \alpha = 0.05$, there are significant differences between the mean age values measured for the two groups, $t = -8.315$; $df = 603$; $p < 0.001$; $M_{\text{Rotavirus (+)}} = 2.54$ years; $M_{\text{Rotavirus (-)}} = 4.34$ years; $M_{\text{dif}} = -1,797$ years; The 95% Confidence Interval (CI) for the difference is (-2.22, -1.37) years.

When we compared the mean value of days of hospitalization, we found in the rotavirus group a higher value than in the nonrotavirus group ($p=0.003$). In the rotavirus group, the mean value of hospitalisation days was 6.84 days, with range between 1 and 21 days, as compared with mean age of 5.96 days in nonrotavirus group, with limits between 2 and 15 days (Figure 2). Because $p = 0.003 < \alpha = 0.05$, there were significant differences between the mean days of hospitalization in the two groups, Rotavirus (+) and Rotavirus (-): $t = 3.002$; $df = 178.16$; $p = 0.003$; $M_{\text{Rotavirus (+)}} = 6.84$ days; $M_{\text{Rotavirus (-)}} = 5.96$ days; $M_{\text{dif}} = 0.889$ days; the 95% CI for the difference is (0.30, 1.47) days.

There were no differences between the maximum value of temperature in both studied groups. ($p=0.963$). The maximum temperature in positive

group ranged between 37.5 and 39.2 degrees Celsius, with an average of 37.97 degrees Celsius. In the Rotavirus (-) group, the maximum temperature was between 37.5-38.8 degrees Celsius, with an average of 37.8 degrees (Figure 3); $M_{\text{Rotavirus (+)}} = 37, 9754$ grade, $M_{\text{Rotavirus (-)}} = 37.8010$ grade, $t = 3.532$, $df = 603$, $M_{\text{dif}} = 0.17445$. The 95% CI for the difference was (-0.7745, -0.27144) degrees Celsius. Because $p = 0.963 > \alpha = 0.05$, there were no significant differences between averages.

Regarding number of vomiting per day, we found a higher number of vomiting per day in Rotavirus (+) group than in Rotavirus (-) group; this difference was statistically significant ($p = 0.001$). The maximum number of vomiting/day in the positive group was 7, and in the negative group was 4 (Figure 4); $M_{\text{Rotavirus (+)}} = 1.4871$, $M_{\text{Rotavirus (-)}} = 0.9$, $M_{\text{dif}} = 0.58713$, $t = 5.907$, $df = 173.82$, 95% CI for the difference is (0.39094, 0.78332). Because $p = 0.001 < \alpha = 0.05$, there were significant differences between groups.

When we took into consideration the comparison between the number of stools per day, we noticed that the number of stools was higher in patients with rotavirus than in those with nonrotavirus gastroenterocolitis, statistically significant ($p=0.001$). The maximum number of stools per day in the positive group was 10, and in the negative group was 6 (Figure 5); $M_{\text{Rotavirus (+)}} = 5.1109$, $M_{\text{Rotavirus (-)}} = 4.21$, $M_{\text{dif}} = 0.90089$, $df = 250.2$, $t = 10.67$, 95% CI for difference is (0.73468, 1.0671). Since $p = 0.001 < \alpha = 0.05$, there were significant differences between groups.

The risk of having patients with vomiting in the Rotavirus (+) group was 6 times higher than the risk of having vomiting in the Rotavirus (-) group [OR = 6; 95% CI for OR is (3.80, 9.46)].

The proportion of patients who had vomiting in the Rotavirus (+) group was twice as high as the

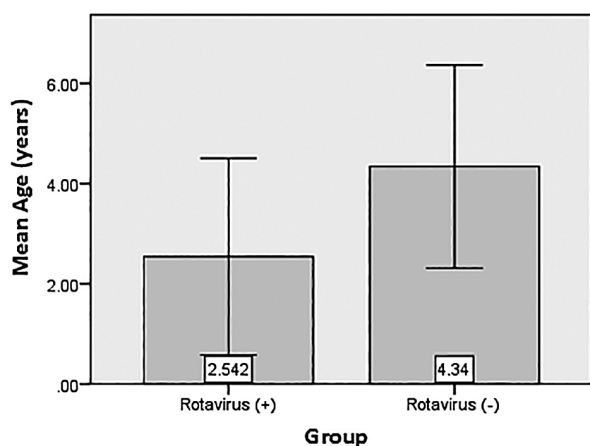


Figure 1. Mean age – comparison between the two groups.

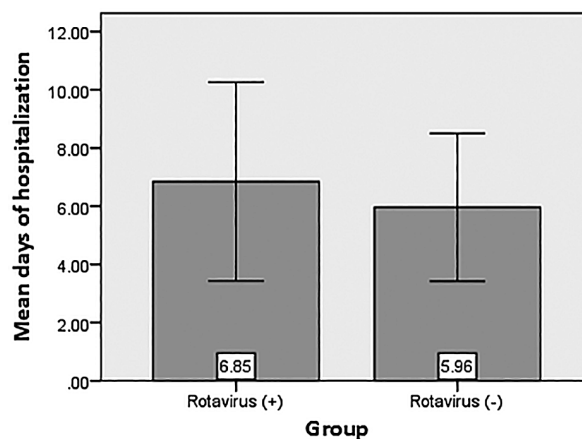


Figure 2. Mean period of hospitalization – comparison between the two groups.

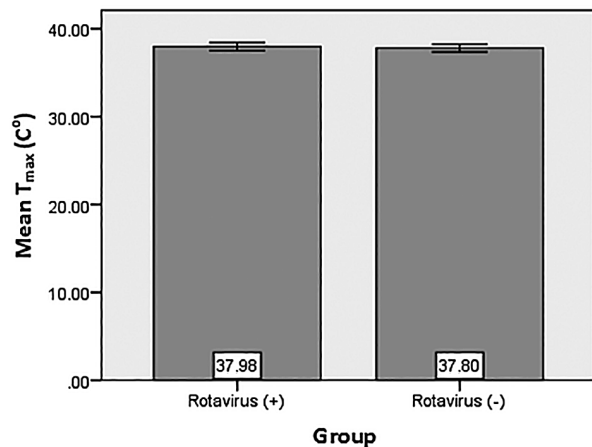


Figure 3. Value of maximum temperature – comparison between the two groups.

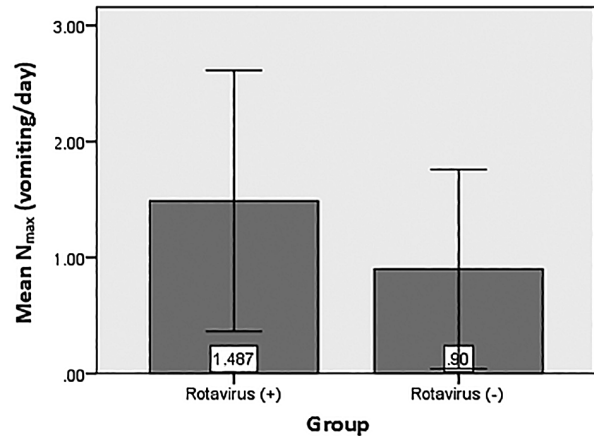


Figure 4. Maximum number of vomiting/day – comparison between the two groups.

proportion of patients with vomiting in the Rotavirus (-) group [RR = 2; 95% CI for RR is (1.56, 2.55)].

The risk of having patients with fever in the Rotavirus (+) group was 3.12 times higher than in the Rotavirus (-) group [OR = 3.12; 95% CI for OR is (1.56; 9.46)].

The proportion of patients with fever in the Rotavirus (+) group was approximately the same as in Rotavirus (-) group [RR = 1.105; 95% CI for RR is (1.019, 1.19)].

The risk of having more than 6 diarrhea stools per day in the positive Rotavirus group was 20.7 times greater than the risk of having more than 6 diarrhea stools per day in the negative Rotavirus group [OR= 20.7; 95% CI for OR is (5.04; 85.05)].

The proportion of patients with more than 6 stools per day from group 1 was 14.85 times higher than the proportion of patients with more than 6 stools per day from group 2 [RR = 14.85; 95% CI for RR (3.74; 58,94)].

The risk of having patients with toxic condition in the positive Rotavirus group was 1.78 times higher than the risk of having patients with toxic condition in the negative Rotavirus group [OR=1.784; 95% CI for OR is (1,045; 3,046)].

Thus, the proportion of toxic cases in the positive Rotavirus group was 1.55 times higher than those with toxic condition in the negative Rotavirus group [RR= 1.55; 95% CI for RR is (1.01; 2.37)].

The risk of having patients with more than 4 vomiting per day in the positive Rotavirus group was 2.55 times higher than those with more than 4 vomiting per day in the negative Rotavirus group [OR= 2.55; 95% CI for OR is (1.595; 10.952)].

The proportion of patients with more than 4 vomiting per day in the positive Rotavirus group was 2.47 times higher than those with more than 4

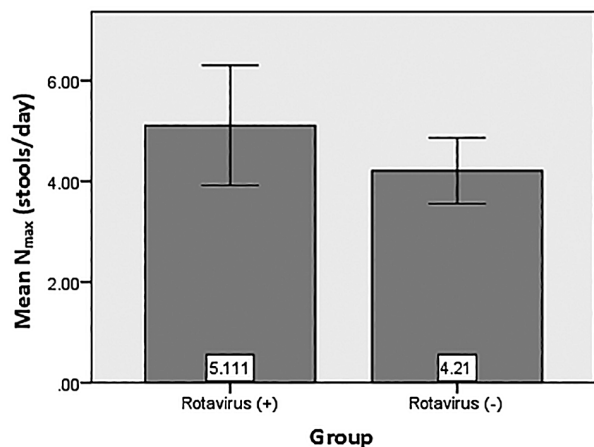


Figure 5. Number of stools – comparison between the two groups.

vomiting/ day in the negative Rotavirus group [RR = 2.47; 95% CI for RR is (1.596; 10.28)].

DISCUSSION

Like in other parts of the world, Rotavirus disease in Romania represents an important public health issue. Excepting deaths, the burden of the disease is similar to that described in the developing world.^{1,2}

Regarding repartition by season, we noticed that in our study and in another one performed in Bucharest, Romania, the most frequent cases were hospitalised during spring (March-May)³, in contrast with studies from other countries, which have found more frequent cases in winter (December-February).⁵ Compared with other studies from Romania, rotavirus infection was more frequent in boys, in our study; Rotavirus gastroenteritis was more frequent

in girls in Bucharest areas.³ The mean age of patients from our study was 2 years, like in other international studies^{5,7}, but lower than that reported in studies performed in another hospital of infectious diseases from Romania³.

The incidence of nosocomial Rotavirus infection in our study, like in other studies performed in Romania, was between 19%- 20%.³

In a study performed in Bucharest, the univariate analysis of 10 characteristics of patients with positive rotavirus gastro-enterocolitis identified 5 associated significant conditions ($p < 0.05$): hypoglycemia, hepatocytolysis, hospitalization longer than 6 days, relapses and dehydration.⁸ Our results confirm some general characteristics of Rotavirus diarrhea from other studies performed in Romania or other countries, such as children age less than 5 years, and degree of dehydration more severe than in other forms of diarrhea^{3, 4, 8, 9, 10}.

Regarding severity of symptoms, such as dehydration, high fever, vomiting and number of stools, these were described in our study, but also in other studies performed in Europe or worldwide⁸⁻¹⁴.

The severity of diarrhea with rotavirus reported in international studies has contributed to the introduction of anti-rotavirus vaccination initially in industrialized rich countries, then in other countries, over the last years. Although the anti-rotavirus vaccine is available in Romania, in order to have an impact on the decrease of hospitalization days due to this disease, it is necessary to introduce this vaccination on large-scale, within the National Immunization Program.

CONCLUSION

In our study, Rotavirus gastroenteritis was more frequent in children less than 5 years old (86.47%) and during the spring (40.8%).

Comparatively with non-Rotavirus diarrhea, gastroenteritis with Rotavirus causes a more severe degree of dehydration, high fever, more watery stools and vomiting and a prolonged period of hospitalisation.

Because of high contagiousness, nosocomial diarrhea with Rotavirus was found in 19.4% from the total number of patients included in the study.

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