

Characteristics of Rotavirus Gastroenteritis in Hospitalized Children in Israel

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ABSTRACT: **Background:** Diarrhea is a leading cause of child mortality worldwide. Rotavirus is one of the most common causes of severe diarrhea and dehydration in children.

Objectives: To compare the demographic, clinical and laboratory characteristics of patients with rotavirus gastroenteritis to those with other causes of gastroenteritis.

Methods: The medical records of children aged 0–18 years hospitalized with acute gastroenteritis in our facility between 1 January 2004 and 31 March 2006 were retrieved. Patients with rotavirus gastroenteritis were compared with patients who were rotavirus negative.

Results: The study group comprised 533 patients; 202 tested positive for rotavirus and 331 tested negative. Compared to patients with rotavirus-negative gastroenteritis, patients with rotavirus-positive gastroenteritis had a higher incidence of vomiting (185/202 vs. 212/331, 92% vs. 64%, $P < 0.001$), lethargy (67/202 vs. 51/331, 33% vs. 15%, $P < 0.001$), and dehydration (81/202 vs. 78/331, 40% vs. 24%, $P < 0.001$). The need for intravenous rehydration therapy and the duration of hospitalization were higher in patients with rotavirus gastroenteritis.

Conclusions: Vomiting and dehydration are more common in hospitalized children with rotavirus gastroenteritis than in children with gastroenteritis due to other causes.

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KEY WORDS: children, gastroenteritis, rotavirus

Diarrhea is a leading cause of child mortality worldwide. Rotavirus is one of the most common causes of severe diarrhea and dehydration in children. It has been estimated that every year 114 million children under the age of 5 years suffer from rotavirus gastroenteritis [1]. Rota infections are more common during the winter months and tend to be more severe in the age range 3–24 months. The route of infection is fecal-oral, with a very low infecting dose needed for infection [2,3].

Previous studies around the world estimated that rota infections are responsible for 30–40% of hospital admissions due to gastroenteritis, and that it causes longer and

more severe disease than diarrhea of other etiologies [2–6]. Rotavirus was detected in 49% of the stool samples taken from children suffering from acute gastrointestinal symptoms in four pediatric clinics in Israel [7]. In two other studies conducted in Israel [8,9] the incidence of rotavirus gastroenteritis was 14–18%. In both those studies no comparison was made between the clinical disease caused by rotavirus and disease due to other infectious causes. Furthermore, there are no data concerning the epidemiological and laboratory findings characterizing rotavirus gastroenteritis.

The aim of the current study was to assess the prevalence of rota infections in hospitalized children in one medical center in Israel. We also aimed to better describe the epidemiological, clinical and laboratory characterizations of rotavirus gastroenteritis compared to gastroenteritis due to other infectious causes.

PATIENTS AND METHODS

We conducted a retrospective chart review of patients admitted with acute gastroenteritis to the pediatric ward. The study was approved by the Institutional Ethics Board of our institution, a university-affiliated hospital in central Israel.

The study group included all patients aged 0–18 years hospitalized between 1 April 2004 and 31 March 2006 with a diagnosis of acute gastroenteritis, rotavirus gastroenteritis, acute diarrhea, or diarrhea and vomiting. Patients were only included if they had been tested for rotavirus. Stool cultures for pathogenic bacteria were taken from all patients. Patients were excluded if they had diarrhea lasting more than 7 days (making the diagnosis of infectious gastroenteritis less reasonable), inflammatory bowel disease or other chronic disease causing diarrhea, were hospitalized for intoxication, or had malformations of the gastrointestinal tract.

Patients were identified through the computerized ward log book. Data were extracted from the patient charts by a single investigator and entered into a database that included information about patients' demographics, clinical variables, laboratory findings and rotavirus test results. Demographic data included age, gender, nationality, area of residence, number of family members, and attendance at an educational institution. The clinical variables were number of hospitalization days,

dehydration, diarrhea characteristics (number per day, number of days with diarrhea), vomiting, state of consciousness, convulsions, vital signs, weight, temperature, other sick family members, nutrition, and treatment in the hospital (antibiotics and intravenous fluids). The laboratory parameters included electrolytes, glucose, uric acid, acid-base disturbances, liver function test, complete blood count, and stool cultures. The patient's clinical condition (e.g., dehydration, lethargy) was defined based on the attending pediatrician's clinical impression. The cases were divided into two groups: rotavirus-positive gastroenteritis and rotavirus-negative gastroenteritis.

The laboratory test used during the study period was RotaStick™ (Novamed, Jerusalem, Israel), a rapid immunochromatographic test. Direct microscopy of the stool was conducted by pediatric residents.

STATISTICAL ANALYSIS

Patients with rotavirus gastroenteritis were compared to patients with other causes of gastroenteritis using the chi-square test for categorical variables and Student's *t*-test or Mann-Whitney test, as appropriate, for continuous variables. *P* < 0.05 was considered significant. Patients with a missing value for any variable were omitted from analysis of the specific variable.

Multivariate logistic regression analysis was used to identify variables associated with increased likelihood for rotavirus gastroenteritis. The multivariate analysis was conducted separately for epidemiological and clinical variables. Age less than one year was included in both analyses. Variables were included in the model if they met a significance level of 0.1 in the univariate analysis.

RESULTS

Of the 780 patients identified through the computerized database, the charts of 765 (98%) were available for review. Based on the exclusion criteria, 232 cases were excluded due to the specified criteria, missing data, or patients who were not tested for rota in the stools. The final analysis comprised 533 patients: 202 cases of RPG, and 331 RNG. The demographic features, clinical characteristics and laboratory findings of the study population are listed in Table 1.

DEMOGRAPHIC VARIABLES

The mean age of the study population was 21.7 months (± 31). Patients with RPG were younger than those with RNG (13.4 ± 9.9 and 26.7 ± 37.8 months respectively, *P* = 0.027). The incidence of RPG was significantly higher during the period October to January as compared to the rest of the year, while the incidence of RNG remained much the same all year round (*P* < 0.001). Thirty-seven patients (18.3%) with

Table 1. Epidemiological and clinical variables of patients with rotavirus-positive and negative gastroenteritis

Variable	RNG (n=331)	RPG (n=202)	OR (reference 1.00 in RNG)	95% CI	P value
DEMOGRAPHIC					
Median age (mos)	14	12			0.027
History of prematurity	40 (12%)	20 (9%)	0.8	0.45–1.4	0.52
History of failure to thrive	22 (7%)	13 (6%)	0.92	0.45–1.84	0.95
Female gender	147 (44%)	87 (43%)	0.94	0.66–1.33	0.81
Moslem origin	84 (25%)	38 (19%)	0.68	0.44–1.04	0.1
Attendance at educational or daycare facility before clinical disease	119 (36%)	53 (26%)	0.69	0.46–1.03	0.09
No. of family members (median)	4	4			0.31
Sick sibling	31 (9%)	37 (18%)	2.16	1.3–3.6	0.004
CLINICAL					
No. of days of illness before admission (median)	1	2			0.06
Systolic blood pressure (median, mmHg)	100	100			0.58
Pulse (average)	135.7 ± 25	139 ± 21			0.13
Weight on admission (median, kg)	9.72 kg	9.04 kg			0.02
Lethargy	51 (15%)	67 (33%)	2.72	1.79–4.13	< 0.001
Fever >38°C	245 (74%)	158 (78%)	1.26	0.83–1.91	0.32
Max. temperature (median, °C)	39	38.95			0.27
No. of days fever > 38°C (median)	1	1			0.44
Vomiting	212 (64%)	185 (92%)	6.49	3.73–11.27	< 0.001
No. of days vomiting (median)	1	2			<0.001
Watery diarrhea	157 (47%)	138 (68%)	1.86	1.27–2.74	0.002
Leukocytes in stool	113 (34%)	55 (27%)	0.58	0.39–0.85	0.008
Blood in stool	29 (9%)	3 (1%)	0.13	0.04–0.42	< 0.001
Maximun no. of stools per day (median)	6	5			0.05
Convulsions	30 (9%)	7 (3%)	0.36	0.16–0.82	0.02
Dehydration	78 (24%)	81 (40%)	2.17	1.49–3.17	< 0.001
IV fluid treatment	249 (75%)	187 (92%)	4.06	2.28–7.21	< 0.001
No. of days IV fluid therapy (median)	1	2			< 0.001
Antibiotic treatment during hospitalization	139 (42%)	67 (33%)	0.69	0.48–0.99	0.053
Duration of hospitalization (median, days)	3	4			0.001

RPG had a sick sibling during the days before admission as compared to 31 patients (9.3%) with RNG (*P* = 0.004).

CLINICAL VARIABLES

Vomiting was more common in patients with rota-positive gastroenteritis than in patients in the RNG group (185 vs. 212, 92% vs. 64%, *P* < 0.001). A higher percentage of patients with RPG suffered from dehydration (81 vs. 78, 40% vs. 24%, *P* < 0.001)

RPG = rotavirus-positive gastroenteritis
RNG = rotavirus-negative gastroenteritis

and had altered mental status (67 vs. 51, 33% vs. 15%, $P < 0.001$). Convulsions occurred in 29 of the 331 patients with RNG (9%) compared to 7 of the 202 RPG patients (3.5%) ($P = 0.02$).

Intravenous fluid therapy was administered to 186 patients with RPG (92%) and 248 patients with RNG (75%) ($P < 0.001$). Patients with RPG required longer hospitalization (median 4 days) than those with RNG (median 3 days) ($P < 0.001$).

LABORATORY VARIABLES

There were only minor non-significant differences in the laboratory findings between the two groups.

MULTIVARIATE ANALYSIS

In the multivariate analysis of demographic variables we included ethnicity, age under one year, presence of a sick sibling at home, and attendance at a daycare center in the days prior to admission. None of the variables was significantly associated with RPG.

The multivariate analysis of clinical variables included vomiting, lethargy, dehydration, convulsions, and age under one year. The presence of vomiting (odds ratio 5.84, 95% confidence interval 3.27–10.46), dehydration (OR 1.66, 95% CI 1.1–2.51) and lethargy (OR 2.22, 95% CI 1.41–3.48) were found to be significantly higher in the RPG patients.

COMPLICATIONS DURING HOSPITALIZATION

During hospitalization there were several patients in both groups who suffered complications. Two patients with RPG and 6 patients with RNG ($P = 0.71$) had bacteremia. In the RPG group 7 patients had elevated liver enzymes, 13 had hypokalemia (of whom one had typical electrocardiographic changes), one patient developed an apparent life-threatening event requiring observation in an intensive care unit, and one infant died. That patient was a 3.5 month old male born at 29 weeks gestation. He was admitted to the hospital suffering from diarrhea and dehydration, and his stool tested positive to rotavirus. Bacterial stool cultures were negative. After 2 days of hospitalization his condition deteriorated; he developed severe metabolic acidosis and was transferred to the pediatric ICU. A few hours later he developed respiratory failure and died later that day. In the RNG group there was 1 patient with syncope, 11 patients requiring intensive care treatment, 16 patients with hypokalemia (of whom 2 had typical ECG changes), 1 patient with intussusception, 2 patients with hepatitis, 2 with neutropenia, and 1 patient developed an abdominal abscess.

BACTERIAL PATHOGENS

Stool cultures were positive in 61 (19%) of the patients in the RNG group compared to 11 (5.5%) in the RPG group ($P < 0.001$).

OR = odds ratio
CI = confidence interval
ICU = intensive care unit

DISCUSSION

In this large cohort of children admitted to hospital with gastroenteritis we found that rotavirus infection was associated with a more severe clinical course than gastroenteritis from other causes. Patients with rotavirus gastroenteritis suffered more often from vomiting, dehydration and altered mental status. They were more likely to require intravenous fluid treatment and were hospitalized for longer periods. Albano et al. [6] reported similar findings among Italian children.

Since rotavirus causes a more severe disease, often necessitating relatively prolonged hospitalizations, it imposes a significant burden on the health system. These findings are even more significant in view of the high incidence of rotavirus infections [10].

Of the 533 children with gastroenteritis included in our study, 37.9% were due to rotavirus. This high percentage correlates with other studies conducted around the world but is twice as high as the incidence reported in another study conducted in six medical centers in Israel [8]. This difference may be attributed to the fact that our study included only hospitalized children, while the study by Grisaru-Soen and colleagues [8] also included ambulatory patients seen in emergency departments. Furthermore, only 533 of 691 cases of gastroenteritis admitted to the hospital in our study were tested for rotavirus, a fact that might also have contributed to the difference in the rotavirus rate between the studies.

The higher rate of rotavirus infections during the winter months compared to the rest of the year is also in accordance with the findings of other studies [3,11].

Several clinical features – such as vomiting, altered mental state and the need for intravenous rehydration – were more common in patients with RPG. These findings remained significant in a multivariate analysis, suggesting that these differences are not due to differences in patient age. These findings are consistent with findings from previous studies. Among Israeli children with gastroenteritis [7] the incidence of vomiting was higher in those who tested positive for rotavirus. In a prospective study from France [12] the duration of hospitalization was longer and the need for intravenous rehydration higher in children with RPG compared to children with other causes of gastroenteritis. In a study of Italian children hospitalized for gastroenteritis, Colomba et al. [1] found that rotavirus was the leading cause of prolonged hospitalization.

The only epidemiological variable found to be significantly different between patients with RPG and patients with RNG was the presence of a sick sibling in the family at the time of presentation. However, in a multivariate analysis that difference did not reach statistical significance, implying that epidemiological data have limited value in suggesting the diagnosis of RPG.

Apart from the obvious differences in the results of stool cultures and rotavirus immunoassay, the laboratory findings

in both groups were similar and hence of no value as a tool to differentiate rotavirus and non-rotavirus infectious gastroenteritis. The incidence of complications during hospitalizations was similar in both groups.

Rotavirus causes around 500,000 deaths each year in the developing world [14], whereas in the developed countries death is a rare complication of rotavirus gastroenteritis. Nevertheless, it still occurs in cases of severe dehydration with severe acidosis, as was the case with one child in our study.

In comparison with other infectious causes of gastroenteritis, rotavirus was not associated with more severe complications among hospitalized patients. However, it was associated with a higher incidence of dehydration and longer hospitalization.

The high burden of the disease led to the development of vaccinations against rotavirus; these proved to be safe and efficient in preventing rotavirus gastroenteritis [15,16]. Several studies have shown that immunization of young infants is cost-effective. It is further hoped that the widespread introduction of immunization will lower the incidence of rotavirus gastroenteritis and related hospitalizations.

As a retrospective study, this study has two major limitations: first, the data extracted from files sometimes lacked details. The second is that since not all patients with gastroenteritis were tested for rotavirus, the true incidence rate of RPG might have been lower. Since there were no specific criteria for testing for rotavirus it is possible that patients who were not tested had a milder disease. Another limitation of this study is the fact that clinicians did not use an objective tool such as dehydration score to assess dehydration. An intra-observer variation could have had an effect on the results.

CONCLUSIONS

In a large cohort of Israeli children with gastroenteritis, rotavirus was responsible for approximately 40% of admissions to the pediatric ward. Younger age and admission during the winter months were more likely to be associated with RPG. Other epidemiological and laboratory tests are not helpful in identifying patients with RPG. Compared to other infectious causes of gastroenteritis, rotavirus is associated with a more severe clinical disease.

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“Management – doing things right; leadership – doing the right things”

Peter Drucker (1909-2005), American writer, management consultant, and self-described “social ecologist.” His writings have predicted many of the major developments of the late twentieth century, including privatization and decentralization, the rise of Japan to an economic world power, the decisive importance of marketing, and the emergence of the information society with its necessity of life-long learning