

The burden of Rotavirus gastroenteritis among hospitalized pediatric patients in a tertiary referral hospital in Jeddah

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BACKGROUND AND OBJECTIVES: To evaluate the burden of Rotavirus gastroenteritis (GE) among pediatric hospital admissions.

DESIGN AND SETTINGS: This is a retrospective observational study, in which all pediatric cases admitted to one of the biggest tertiary hospitals in Jeddah, with the diagnosis of GE, in the year 2010, were enrolled.

PATIENTS AND METHODS: This is a retrospective observational study in which all pediatric cases admitted with the diagnosis of GE in the year 2010 were enrolled. Clinical data and laboratory findings were compared between Rota positive and Rota negative cases. The data was statistically analyzed.

RESULTS: GE cases represented 8.8% of all pediatric hospital admissions in 2010. Almost 43% (42.9%) of these cases proved to have Rotavirus GE. Rotavirus infection alone, adenovirus infection alone, combined Rotavirus and adenovirus infection, and other causes of GE were present in 101 (33.6%), 21 (7%), 28 (9.3%), and 151 (50.2%) patients respectively. Coinfection with adenovirus was higher in Rota-positive GE (RPG; $P=.039$). Vaccination against Rotavirus was protective against Rotavirus GE ($P=.042$).

CONCLUSIONS: Rotavirus infection is the most important causative organism of GE in our community that accounted for 42.9% of children hospitalized for GE in our study, either alone or with other infections. Among our patients, vaccination against Rotavirus appeared to be protective against Rotavirus GE. In view of the high disease prevalence among children, locally and worldwide, we recommend routine Rotavirus vaccination as the most effective available means of control despite improvement in sanitation and hygiene.

Rotavirus has been recognized as a cause of severe diarrhea in children worldwide, a major cause of morbidity in the developed world, and a cause of both morbidity and mortality in the developing world.¹ Despite marked improvements in water quality, sanitation, and hygiene, the fact that the incidence of Rotavirus diarrhea has not decreased substantially during the past decade suggests that immunization may be the most promising preventive strategy.²

Two oral, live, attenuated Rotavirus vaccines, Rotarix (GlaxoSmithKline Biologicals, Belgium) and RotaTeq (Merck & Co. Inc., USA), are available internationally, and both vaccines are considered safe and effective in preventing gastrointestinal diseases caused by Rotaviruses.

WHO recommends that Rotavirus vaccine for infants should be included in all national immunization

programs as an important measure to reduce severe Rotavirus-associated diarrhea and child mortality. The use of Rotavirus vaccines should be part of a comprehensive strategy to control diarrheal diseases. This strategy should include, among other interventions, improvements in hygiene and sanitation, zinc supplementation, community-based administration of oral rehydration solution, and overall improvements in case management. WHO recommends that Rotavirus vaccine for infants should be included in all national immunization programs.³

Aim of the study

To evaluate the burden of Rotavirus gastroenteritis (GE) among pediatric hospital admissions in one of the biggest private tertiary hospitals in Jeddah and the western region of Saudi Arabia.

PATIENTS AND METHODS

This is a retrospective observational study in which all the pediatric cases, admitted with a diagnosis of GE in the year 2010, were studied. Pediatric cases, as per our hospital policy, are defined as patients younger than 14 years old. This involved the study of the clinical data of all enrolled patients including history (with special attention to vaccination history), duration of hospitalization, clinical presentation, and complications. The degree of dehydration was assessed on admission and graded as mild (3%-5% volume loss), moderate (6%-9% volume loss), or severe ($\geq 10\%$ volume loss).⁴ The complications, recorded in the patients' medical records,

included electrolyte imbalance in the form of hypernatremia, and renal impairment in the form of elevated blood urea nitrogen and serum creatinine. The laboratory findings including complete blood (add cell) count (CBC), C-reactive protein (CRP), electrolytes, stool analysis for ova or parasites, stool viral analysis for both Rotavirus and Adenovirus, and stool culture were studied in all cases. Stool viral analysis was performed by enzyme immunoassay (Premier Rotaclone, Meridian Bioscience Inc., USA). The sensitivity, specificity, positive predictive value, and negative predictive value for Rotaclone are 100, 99, 99, and 100%.⁵ A comparison between Rota positive cases and Rota negative cases

Table 1. Demographic, clinical, and laboratory data of Rota positive and Rota negative patients.

		RPG	RNG	Total	P value
Number (%)		129 (42.9%)	172 (57.1%)	301 (100%)	
Age (mo)		30.3 (21.6)	41.3 (34.4)		.001 ^a
Sex	Female	62 (48.1%)	82 (47.7%)	144 (47.8%)	1.000
	Male	67 (51.9%)	90 (52.3%)	157 (52.2%)	
Rota vaccination	Vaccinated	3 (2.3%)	14 (8.1%)	17 (5.6%)	.042 ^a
Symptoms	Fever	87 (67.4%)	114 (66.3%)	201 (66.8%)	.902
	Vomiting	127 (98.4%)	165 (95.9%)	292 (97.0%)	.309
	Diarrhea	127 (98.4%)	158 (91.9%)	285 (94.7%)	.017 ^a
Dehydration		129 (100.0%)	169 (98.3%)	298 (99.0%)	.263
Degree of dehydration	Mild	14 (10.9%)	32 (18.6%)	46 (15.3%)	.079
	Moderate	48 (37.2%)	65 (37.8%)	113 (37.5%)	
	Severe	67 (51.9%)	72 (41.9%)	139 (46.2%)	
	None	0 (0.0%)	3 (1.7%)	3 (1.0%)	
Complications	Hypernatremia	1 (0.8%)	0 (0.0%)	1 (0.3%)	.133
	Renal impairment	2 (1.6%)	0 (0.0%)	2 (0.7%)	
Adenovirus in stools	Adeno neg	101 (78.3%)	151 (87.8%)	252 (83.7%)	.039 ^a
	Adeno pos	28 (21.7%)	21 (12.2%)	49 (16.3%)	
Stool protozoa or parasites	Entamoeba histolytica	1 (0.8%)	8 (4.7%)	9 (3%)	.356
Stool culture results	No pathogen	126 (97.7%)	163 (94.8%)	289 (96.0%)	.618
	Pseudomonas aeruginosa	1 (0.8%)	1 (0.6%)	2 (0.7%)	
	Salmonella	2 (1.6%)	8 (4.6%)	10 (3.3%)	
Hospital stay (d)		1.9 (0.8)	2.0 (0.9)		.599
CRP (mg/dL)		2.4 (4.6)	3.7 (6.3)		.004 ^a

^aStatistically significant.

Note: Data are reported as either numerical (%) or mean (SD).

was done regarding demographic, clinical, and laboratory data. Burden of Rota-positive GE (RPG) was assessed based on the percentage of RPG to all pediatric hospital admissions, duration of hospitalization, and complications. Approval of our hospital research and ethical committee was taken. Cases with preliminary diagnosis of GE and with proofs of other symptoms as systemic cause of GE, chronic diarrhea, or others were excluded. Data were statistically described in terms of mean (standard deviation [SD]), or frequencies (number of cases) and percentages when appropriate. Comparison of numerical variables between the study groups was done using t test for independent samples. For comparing categorical data, chi-square (2) test was performed. Exact test was used instead when the expected frequency was less than 5. *P* values less than .05 was considered statistically significant. All statistical calculations were done using computer programs SPSS, version 15 (Chicago, Illinois).

RESULTS

The total pediatric hospital admissions in the year 2010 were 3424 patients. GE case represented 8.8% of these (301 patients).

Table 1 shows the demographic, clinical, and laboratory data of all cases. Of the 301 patients enrolled, 129 (42.9%) proved to have RPG and 172 (57.1%) had Rota-negative GE (RNG) (**Table 1**). RPG constituted 3.8% and RNG constituted 5% of the total hospital pediatric admissions in 2010. Rotavirus infection alone, adenovirus infection alone, combined Rotavirus and adenovirus infection, and other causes of GE were present in 101 (33.6%), 21 (7%), 28 (9.3%) and 151 (50.2%) patients, respectively (**Figure 1**).

Co-infection with adenovirus was higher in RPG (21.7%) than in RNG (12.2%), and this showed statistical significance (*P*=.039). Co-infection with other organisms, however, whether protozoa or bacterial infections, did not show statistical difference between both groups (**Table 1**).

RPG was present all through the year with the highest peak in November, a lower peak in April, and the lowest peak in August, denoting an increased incidence in autumn and spring months (**Figure 2**).

RPG was present in younger ages (30.33 [21.620] months) as compared to RNG (41.36 [34.402] months), and this was statistically significant (*P*=.001) (**Table 1 and Figure 3**).

Our laboratory results showed no statistically significant difference between both groups regarding the results of CBC or electrolytes. However, CRP results were significantly lower in RNG group.

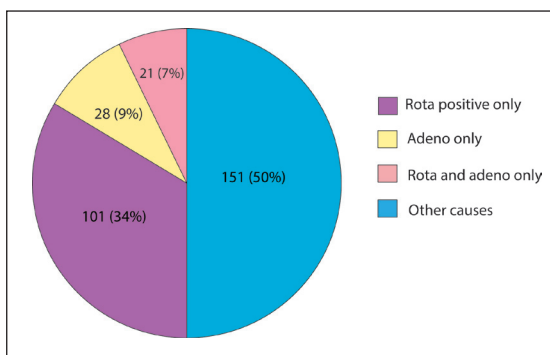


Figure 1. Causes of gastroenteritis among enrolled patients (number, percentage).

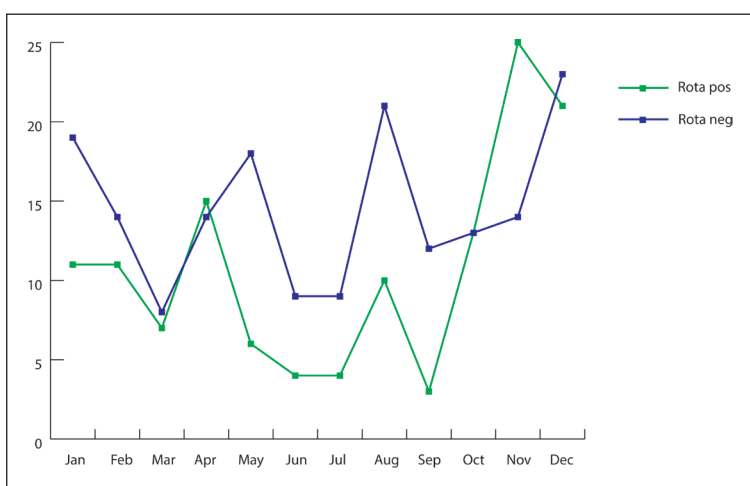


Figure 2. Distribution of patients over the year.

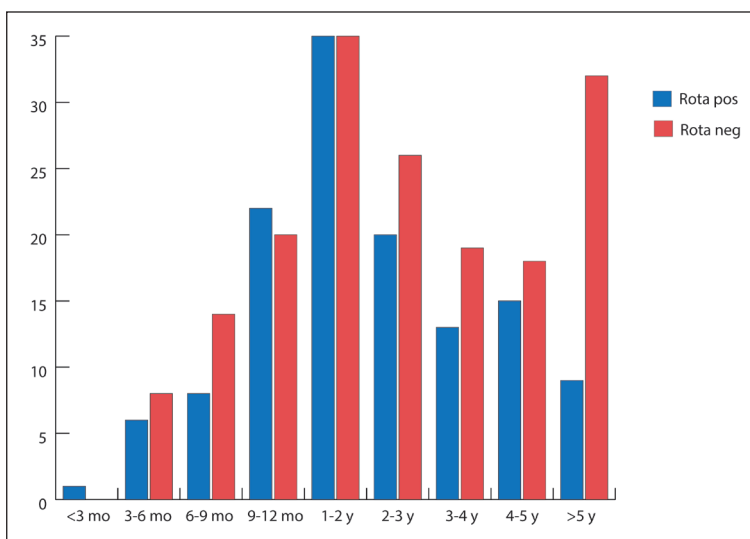


Figure 3. Age distribution of patients.

Our results suggest the protective value of Rotavirus vaccination with a statistically significant difference between both groups ($P=.042$) although the number of vaccinated children was small in both groups. Fourteen children (8.1%) were vaccinated among RNG patients and only 3 (2.3%) among RPG patients (Table 1). Vaccinated children received two doses of Rotarix (GlaxoSmithKline Biologicals, Belgium; human, live attenuated monovalent Rotavirus vaccine).

DISCUSSIONS

Rotavirus is the cause of more than 2 million hospitalizations and over half a million deaths from acute GE in infants and young children worldwide, especially in developing parts of the world such as Africa and Asia, where 85% of Rotavirus deaths occur.¹

In our study, all GE cases constituted 8.8% of the total pediatric hospital admissions in the year 2010 (Figure 1). Rota positive cases accounted for 3.8% of the total pediatric hospital admissions and 42.9% of all pediatric cases admitted for GE (Figure 1 and Table 1). Different studies were conducted to estimate the prevalence of GE among Saudi children, and these studies showed results similar or close to ours. In a review of 22 published studies of Rotavirus and the etiology of diarrhea carried out from 1982 to 2003, the prevalence of Rotavirus infection ranged from 10% to 46% with a median of 30%.⁶ Another study showed that Rotavirus was the pathogen most frequently detected among children with GE in Saudi Arabia, either alone (44.3%) or in combination with other enteropathogens (7%).⁷ Other studies conducted in Jeddah, which is the same city of our current study, showed prevalence rates of 34.6%, 41.3%, and 46%.⁸⁻¹⁰ A lower prevalence rate was detected in other regions of Saudi Arabia. Rotavirus was detected in 10% of GE cases in a study done in Makkah. This could be due to the geographical location of Makkah with very hot and dry summer, and mild winter and almost no rain throughout the year.¹¹ Similarly, different results were shown in other regions of Saudi Arabia, 11.5% in the Eastern Province, 23.7% in Dammam and 12% in Gizan.¹²⁻¹⁴

In the Middle East and North Africa region, the annual proportion of RPG among reported episodes of pediatric GE was 42%.¹⁵ However, when Middle Eastern and North African countries were compared with each other, large variations in proportion of RPG estimates were observed, with a low of 16%-23% reported in Saudi Arabia, Tunisia, and Egypt, and a high of 44%-61% in Syria, Oman, and Kuwait.¹⁶ Epidemiological surveys worldwide showed variable results. The incidence of Rotavirus causing acute di-

arrhea ranged between 12 and 71%, with an average of 34% in children under 3 years of age.¹⁷ The incidence was found to be between 5 and 71% in India, 12% to 42% in Brazil, 23.4% in Turkey, 24% in Zambia, 40% in Israel and 45.4% in Uganda in two studies done in 1987 and in 2010.¹⁷⁻²³ These results show that the burden of this disease has not changed over the years. It also shows that the incidence of RPG is similar in both developed and developing countries worldwide.

In the current study, there was no statistically significant difference between RPG and RNG patients regarding the gender ($P=1.000$) (Table 1). However, in a previous study performed in Saudi Arabia, as in another Brazilian study, males accounted for higher percentage of all diarrheal cases.^{8,24}

According to the results in our study, RPG was present in younger ages (30.33 [21.620] months) as compared to RNG (41.36 [34.402] months), and this showed statistical significance ($P=.001$) (Table 1). Different studies conducted in Saudi Arabia showed similar results. A review of 22 published studies of Rotavirus in Saudi Arabia in 21 years showed that most cases were among children less than 2 years of age, and particularly in the first year of life.⁶ Other studies performed worldwide confirmed the higher incidence of Rotavirus in younger ages, with the age group most affected between 0 and 1 year olds.²²⁻²⁶

Globally, Rotavirus is more common in the cooler months, but seasonal peaks can vary broadly and may occur from autumn to spring.²⁷ In our study, RPG was present all through the year with the highest peak in November, a lower peak in April, and the lowest peak in August, denoting an increased incidence in autumn and spring months (Figure 3). Earlier studies performed in Jeddah showed an increase in the frequency of infection in the cooler months, which is consistent with our results.^{9,10} A pattern of higher RPG cases was seen in warmer months in Al-Taif.⁹ No significantly different seasonal variation in the prevalence of Rotavirus was shown in another study in Dammam.¹³ These differences could be owed to the vast geographic distribution of Saudi Arabia with different types of weather in different regions. Moreover, many people, from all over the world, come to Saudi Arabia for pilgrimage and employment all through the year. They travel to and fro countries with different weather circumstances and Rotavirus prevalence.

A number of countries in the Middle East reported seasonality data including Egypt, Iran, Libya, Morocco, Oman, Saudi Arabia, Tunisia, and Turkey. For most of these countries, as in different European countries, the peak season for RPG is in winter from November to April.^{16,25}

Hospital stay is usually used as an indicator of the burden of the disease. In the current study, hospital stay was almost the same in both groups. Hospital stay among RNG cases was 2.00 (0.949) days while it was 1.92 (0.806) days among RPG cases ($P=.599$) (Table 1). Data from other countries indicated that RPG among young children required hospitalization of at least 3 days.^{25,28-30}

Regarding the symptomatology of RPG patients, only diarrhea was significantly higher in RPG ($P=.017$) (Table 1) in this study. This was consistent with another study conducted in Brazil, and the results showed that diarrhea was the main presenting symptom.²⁴ However, unlike our study, Perl et al. showed that vomiting was more common in patients with RPG and with high statistical significance.²²

Neither the presence of dehydration ($P=.263$) nor its degree ($P=.079$) showed statistically significant difference between the two groups of our study (Table 1). This could be owed to the fact that the presence of dehydration was the cause of admission to hospital in most of the patients of both groups. Similarly, Perl et al. and Nakawesi et al. showed an increase in both the presence and the degree of dehydration in RPG patients.^{22,23}

None of the RNG group in our study had complications in the form of hypernatremia or renal impairment in contrast to 1 case of hypernatremia and 2 with renal impairment in RPG group. Though this did not show statistical significance ($P=.133$) (Table 1). However, complications like convulsions, bacteremia, elevated liver enzymes, hypokalemia, and death, which were reported by Perl et al. were seen in none of our patients.²²

We did not find statistically significant differences in the laboratory results of both groups except for CRP results. It was significantly less in RPG patients compared to RNG patients ($P=.004$) (Table 1). We can owe this difference to the possibility of bacterial GE among RNG patients that could have led to a higher CRP. Other studies showed only minor nonsignificant differences in

laboratory variables between RPG and RNG cases.²²

In our study, infection with adenovirus was higher in RPG (21.7%) than in RNG (12.2%), and this showed statistical significance ($P=.039$). Rotavirus and adenovirus co-infection was addressed in other studies, and an incidence of 17.9% was shown in a study of GE among Korean children.³¹ Regarding the incidence of other viral infections, we cannot claim that adenovirus is the second most common cause of GE, as the viral tests that are available in our center are only for Rotavirus and adenovirus. A previous study showed statistically higher bacterial co-infection among RPG cases.²²

Our results suggest the protective value of Rotavirus vaccination in spite of the small number of vaccinated children (Table 1). Since the 2006 introduction of live Rotavirus vaccine, hospitalizations for GE during the Rotavirus season have declined markedly in the USA, as have emergency department and physician office visits for GE. Vaccination is considered the most effective way to achieve disease control.³²

In conclusion, Rotavirus infection is the most important causative organism of GE in our community that solely accounted for 42.9% of children hospitalized for GE.

In view of the high disease prevalence among children, locally and worldwide, and in view of the effectiveness of vaccination shown in the previous studies and our study, we recommend routine Rotavirus vaccination as the most effective available means of control despite improvement in sanitation and hygiene. Surveillance for the efficacy and effectiveness of vaccination as well as the differential efficacy of the 2 available vaccines is recommended.

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