

## Rotavirus gastroenteritis among children under five years of age in İzmir, Turkey

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**SUMMARY:** Kurugöl Z, Geylani S, Karaca Y, Umay F, Erensoy S, Vardar F, Bak M, Yaprak I, Özkınay F, Özkınay C. Rotavirus gastroenteritis among children under five years of age in İzmir, Turkey. Turk J Pediatr 2003; 45: 290-294.

Little is known about the epidemiology of rotavirus infection in Turkey. The aim of the study was to determine the incidence and clinical significance of rotavirus gastroenteritis, in view of the potentially available prevention by rotavirus vaccination. The study also sought to determine possible risk factors for rotavirus gastroenteritis. Therefore, 920 children under five years of age with acute gastroenteritis admitted to three pediatric hospitals in İzmir were studied. Rotavirus was identified in 39.8% of the children. Most children with rotavirus gastroenteritis (80.7%) were younger than two years of age. Marked seasonality of rotavirus gastroenteritis was observed, with a peak incidence from January to March. A total of 91% of rotavirus strains that were typed were of serotypes G 1-4. There was no significant difference among rotavirus-positive and rotavirus-negative patients with regard to family income. Compared with children who were exclusively breast-fed, those who were not exclusively breast-fed were at a two-fold greater risk of rotavirus diarrhea. Rotavirus gastroenteritis was significantly more severe than non-rotavirus gastroenteritis; 69% of children with rotavirus infection had severe gastroenteritis (score  $\geq 11$ ).

In conclusion, rotavirus is the most common cause of severe gastroenteritis among children under five years of age in İzmir. A new potent rotavirus vaccine, when available, will provide effective protection against severe rotavirus infection. Promotion of breast-feeding would augment the impact of rotavirus vaccines in preventing severe childhood diarrhea.

*Key words:* epidemiology, risk factors, rotavirus, serotype.

Rotavirus is the most common cause of severe gastroenteritis among children worldwide, resulting in approximately 800,000 deaths each year<sup>1</sup>. Rotavirus is still considered to have infected all children by the age of five years regardless of socioeconomic status or environmental conditions<sup>2</sup>. Because of the disease burden associated with rotavirus and the fact that improvements in hygiene and sanitation have not decreased the incidence of rotavirus gastroenteritis, efforts to develop vaccines against rotavirus have been under way since the 1980s. In 1998, the first rotavirus

vaccine was licensed in the USA and the routine use of this vaccine for the immunization of healthy infants was recommended. However, these recommendations were suspended in July 1999 and withdrawn in October 1999 following the discovery of an association between the vaccine and intussusception<sup>3</sup>. It is now anticipated that new vaccines against rotavirus, without intussusception risk, will be developed. A potent rotavirus vaccine, when available, is considered as effective protection against rotavirus infection. However, before a decision is made on the introduction of the vaccination

for rotavirus in each country, specific national epidemiologic studies and knowledge of current disease burden are required.

A nationwide surveillance system for rotavirus infections in Turkey has not been implemented to date. Little is known about the epidemiology of rotavirus infection<sup>4-6</sup>. There has been no report on the results of serotyping of rotavirus strains. Therefore, this study as planned to assess the incidence and clinical significance of rotavirus gastroenteritis in children under five years of age admitted for acute gastroenteritis in İzmir, Turkey. The study also aimed to determine risk factors that might predispose a child to rotavirus gastroenteritis.

### Material and Methods

The study was conducted prospectively in three pediatric hospitals in İzmir, Turkey. These hospitals (Department of Pediatrics of Ege University Medical School Hospital, Behçet Uz Children's Hospital, and Social Security Tepecik Children's Hospital) serve urban and suburban districts of İzmir. From January 2000 through January 2001, 920 children under five years of age who admitted for acute gastroenteritis were evaluated.

A pediatrician interviewed the parents and completed a questionnaire including information on socio-demographic characteristics. The same pediatrician examined all children and recorded signs and symptoms on a follow-up chart. The symptoms were followed-up regularly and recorded daily on the follow-up chart along with diarrheal episode.

To investigate the effect of breast-feeding on rotavirus gastroenteritis, the children were divided into two subgroups: those who were "exclusively breast-fed" in the first six months of life and those "not exclusively breast-fed".

The severity of acute gastroenteritis was estimated using a 0-20 point scoring system, proposed by Ruuska and Vesikari<sup>7</sup>, based on diarrhea, vomiting, dehydration, fever and need for a medical visit. Cases with scores 1-10 were accepted as clinically mild, and cases with scores of 11 or higher as severe.

Stool specimens were collected from the children on admission. All specimens were cultured for *Salmonella*, *Shigella*, *Campylobacter jejuni*, *Vibrio cholerae*, and *Escherichia coli* by standard

methods. Fresh fecal specimens were examined by light microscopy for parasitic ova and cysts and by the modified acid-fast stain for *Cryptosporidium parvum*.

Rotavirus in the stools was demonstrated using an ELISA kit (IDEIA™ rotavirus test, Dako, United Kingdom). Rotavirus gastroenteritis was diagnosed when rotavirus antigen was detected in the stool of a child with acute gastroenteritis. Non-rotavirus gastroenteritis was defined when rotavirus antigen was not detected in the stool of a child with acute gastroenteritis. Rotavirus-positive specimens were serotyped by reverse transcriptase-polymerase chain reaction (RT-PCR).

Statistical analysis was performed using SPSS 10.0 for Windows (SPSS Inc, Chicago). The characteristics of the patients with rotavirus or non-rotavirus gastroenteritis were compared with chi-square and Student's t tests. Mann-Whitney U test was used to compare rotavirus with non-rotavirus gastroenteritis with respect to severity scores. A p value of <0.05 was considered statistically significant. Odds ratios (Ors) and 95% confidence intervals (CIs) for possible risk factors such as age, prematurity, lack of exclusive breast-feeding in the first six months of life, low family income, and poor hygiene status were calculated for rotavirus gastroenteritis.

### Results

During the one-year study period, 920 children with acute gastroenteritis were recruited. Rotavirus was identified in 366 (39.8%) of the children. Parasites (*Entamoeba histolytica*, *Giardia lamblia*, *Cryptosporidium*) and bacterial enteropathogens (*Shigella*, *Salmonella* spp.) were detected in 99 (10.7%) and 72 (7.8%) cases, respectively. Three hundred and eighty-three cases (41.7%) remained etiologically unresolved.

Among a total of 366 rotavirus-positive stool samples, 324 could be typed by RT-PCR. Of these, 295 (91.1%) were serotype G 1-4. G1 serotype was the most common (75.1%). G 2-4 serotypes were identified in the following proportions: G2 (0.8%), G3 (3%) and G4 (6.3%). Mixed rotavirus infection was identified in 5.9% of the specimens. A total of 8.9% of strains were nontypable.

Children with rotavirus gastroenteritis were younger than patients with gastroenteritis and negative stool rotavirus antigen test: mean age  $15.3 \pm 12.4$  vs  $17.5 \pm 16.7$ , respectively. Most patients with rotavirus gastroenteritis (295/366,

80.7%) were younger than two years (Table I). The detection rate of rotavirus was highest among children 6-23 months of age, in whom it accounted for 46% (237/515) of all gastroenteritis. In children over two years old, rotavirus was identified in only 30.5% (71/233) of the cases. There was a significant difference between the age group of 6-23 months and the age group older than two years ( $p<0.05$ ).

The seasonal distribution of rotavirus gastroenteritis displayed a higher incidence in winter and early spring (Fig. 1). Rotavirus season started gradually in October, peaked in January to March, and lasted until May. In winter months, rotavirus was detected in approximately 60-65% of the cases with acute gastroenteritis. In the summer the proportion of rotavirus gastroenteritis was lower than 20%.

**Table I.** Comparison of Characteristics Between Rotavirus-Positive and Rotavirus-Negative Patients

	No. (%) of children	
	Rotavirus-positive (n=366)	Rotavirus-negative (n=554)
Age (months)		
0-5	58 (15.8)	131 (23.7)
6-11	118 (32.3)	154 (27.8)
12-23	119 (32.5)	124 (22.4)
24-60	71 (19.4)	145 (26.2)
Prematurity	23 (7.1)	31 (5.3)
No source of piped water	15 (4.1)	14 (2.5)
No lavatory in home	7 (1.9)	7 (1.2)
Low income	88 (24.0)	154 (27.8)
Not exclusively breast-fed <sup>1,2</sup>	272 (84.0)	374 (71.6)
Severity score <sup>3</sup>		
< 11	113 (30.9)	337 (60.8)
≥ 11	253 (69.1)	217 (39.2)
Dehydration <sup>3</sup>	164 (44.8)	105 (19.0)
Hospitalization <sup>3</sup>	113 (30.9)	80 (14.4)

<sup>1</sup> Exclusive breast-feeding shorter than six months.

<sup>2</sup>  $p<0.05$ .

<sup>3</sup>  $p<0.01$ .

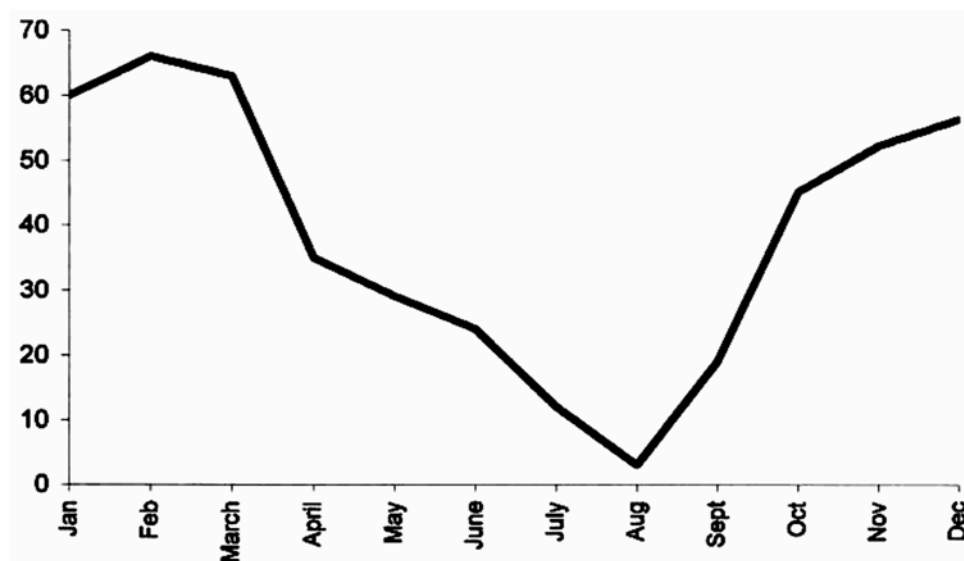


Fig. 1. The seasonal distribution of rotavirus (RV) gastroenteritis.

Premature infants do not have an increased risk for rotavirus gastroenteritis (Table I). Rotavirus-positive patients were nearly identical to rotavirus-negative patients with respect to sex. There was no significant difference among rotavirus-positive and -negative patients with regard to family income. The detection rates of rotavirus in children who had a source of piped water in their homes were similar to those who lacked a source of piped water. There was a significant association between rotavirus diarrhea and being not exclusively breast-fed in the first six months of life ( $p < 0.05$ ). Compared with children who were exclusively breast-fed for six months or longer, those who were exclusively breast-fed for less than six months were at a two-fold greater risk of rotavirus gastroenteritis (OR=2.1, 95%CI= 1.5-2.9).

Among 461 infants under 12 months old, 277 were breast-fed during the study period. Rotavirus was responsible for 49.5% of all diarrheal episodes in infants who were not breast-fed, whereas in infants who were breast-fed rotavirus was detected in only 30.7% of cases (85/277) ( $p < 0.001$ ).

Rotavirus gastroenteritis was significantly more severe than non-rotavirus gastroenteritis (median severity score 13 vs. 9, respectively,  $p < 0.0001$ ). The majority of the children (253/366, 69.1%) with rotavirus gastroenteritis had a score  $\geq 11$ , whereas only 39.2% (217/554) of the children with non-rotavirus gastroenteritis had a score  $\geq 11$  (Table I). Approximately 45% of patients with rotavirus gastroenteritis developed dehydration, a proportion significantly greater than that among those with non-rotavirus gastroenteritis (19%) ( $p = 0.002$ ).

Of the 920 children in the study group, 193 (21%) required hospitalization. The majority of the cases requiring hospitalization (113/193, 58.9%) were associated with rotavirus. The mean hospital stay for rotavirus gastroenteritis was  $5.5 \pm 5.1$  days, and for non-rotavirus gastroenteritis  $3.3 \pm 3.1$  days. Duration of hospital stay for rotavirus gastroenteritis was significantly longer than that for non-rotavirus gastroenteritis.

## Discussion

In the present study, in order to understand the burden of rotavirus gastroenteritis in İzmir, Turkey, we reported the state of rotavirus infection in children under five years of age. Our

findings show that rotavirus is the most commonly detected etiologic agent, being responsible for 39.8% of admissions for acute gastroenteritis. This proportion is higher than that observed in Pakistani children<sup>8</sup> and is similar to reports from England and Wales<sup>9</sup>, Finland<sup>10</sup>, Poland<sup>11</sup>, Vietnam<sup>12</sup> and Peru<sup>13</sup>.

As in most countries with temperate climate, in İzmir, rotavirus gastroenteritis presented a clear seasonal pattern. Rotavirus gastroenteritis appears to be consistently more prevalent in winter, with a peak from January through March. Conversely, rotavirus was rarely detected in summer from June to September.

According to the results of previous studies, the association between rotavirus and severe diarrhea is conflicting. In a hospital-based study in Bangladesh it was reported that children infected with rotavirus had less severe dehydration than those infected with other enteropathogens<sup>14</sup>. Rotavirus was also found not to be associated with severe dehydration in several case-control studies<sup>15-17</sup>. Conversely, some studies reported that rotavirus diarrhea was particularly severe compared with infections by other enteropathogens<sup>10,13,18,19</sup>. In these studies, the authors usually relied on hospitalizations as an indicator of severe rotavirus gastroenteritis. Since admission to a hospital may be influenced by socio-economic factors and/or by the doctor's attitude, we decided to score each gastroenteritis episode using a clinical scoring system. The majority of rotavirus-positive patients (69.1%) in our study had severe gastroenteritis (score  $\geq 11$ ). A new tetravalent rotavirus vaccine effective against severe rotavirus gastroenteritis may prevent most hospital admissions associated with rotavirus in Turkish infants.

In the present study, rotavirus detection rates among children with high and low socioeconomic status were similar. Furthermore, we found similar detection rates among children who did or did not have a source of piped water in the home. These findings indicate that clean water supplies and good hygiene have not decreased the incidence of rotavirus gastroenteritis. Exclusive breast-feeding was found to be significantly associated with a lower incidence of rotavirus gastroenteritis. The low incidence might be due to the antiinfective properties of breast-milk. Promotion of breast-feeding would augment the impact of rotavirus vaccines in preventing severe childhood diarrhea.

In the present study, most cases of rotavirus gastroenteritis were younger than two years of age; they constituted 80.7% of all patients with this disease. It is suggested that the younger group was more easily infected by rotavirus than the older group. Therefore, we recommend early rotavirus vaccination in Turkish infants. Since nearly 50% of patients with rotavirus were younger than one year of age, the impact of the vaccine would diminish if immunization were delayed beyond that age.

Prior to the introduction of rotavirus vaccines in a country, it is important to know which serotypes of rotavirus are currently circulating. In this study, which is the first one reporting the results of serotyping of rotavirus strains in Turkey, 91% of rotavirus strains that were typed were found to be G serotype 1-4. This observation indicates that a tetravalent rotavirus vaccine, which includes rotaviruses of serotype G1-G4, is likely to be effective in reducing the incidence of rotavirus gastroenteritis in İzmir, Turkey.

Rotavirus vaccines may work less well in developing countries than in developed countries, where mixed infections are less common<sup>13</sup>. In the present study, mixed infection was identified in only 5.9% of the specimens, thus rotavirus vaccines may be more effective in İzmir than in developing countries where mixed infections are more common.

In conclusion, rotavirus is the most common cause of acute gastroenteritis in children under five years of age in İzmir. The high incidence of rotavirus and its association with severe gastroenteritis underscore the need to control rotavirus gastroenteritis. A new potent rotavirus vaccine, when available, will provide effective protection against severe rotavirus gastroenteritis. However, more information obtained from epidemiologic studies that will be carried out in other regions of Turkey is needed for a decision on the introduction of a rotavirus vaccine in Turkey.

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