ECRONICON OPEN ACCESS

EC MICROBIOLOGY
Research Article

The Study of Incidence, Clinical Presentation and Progression of Rota Virus Infection in Hospitalized Children with Acute Nonbacterial Diarrhea: A Cross Sectional Study in Tehran, Iran

Samileh Noorbakhsh[1]*, Fahimeh Ehsanipour[1], Farideh Ebrahimi Taj[1] and Zahra Movahedi[2]

[1]*Department Pediatric Infectious Diseases, Iran University of Medical Sciences, Tehran, Iran*

[2]*Department of Pediatric Infectious Diseases, Qom University of Medical Sciences and health services, Qom, Iran*

***Corresponding Author**: Samileh Noorbakhsh, Department Pediatric Infectious Diseases, 4th floor Rasul Akram Hospital, Niayesh Street, Satarkhan Avenue, Tehran, Islamic, Iran.

Received: February 12, 2017; **Published:** March 06, 2017

Abstract

Background: Rotavirus infection is the most common cause of acute diarrhea in children. Main goal of this study was to determine the incidence, clinical presentation and progression of Rota virus infection in hospitalized children with acute non bacterial diarrhea.

Methods: In a prospective cross sectional study, we studied 80 children with acute onset of non bacterial diarrhea in the pediatric ward of Rasoul Akram Hospital (2011-2013), Tehran. The presence of rotavirus antigen in stool were studied.

Results: Thirty nine (48.8 percent) have positive tests for rotavirus. Incidence of rotavirus diarrhea in males was more than female patients, %76.9 of rotavirus diarrhea were observed in cases younger than 18 months. Also, degree of dehydration in children with rotavirus diarrhea was more severe than other cases.

Conclusion: Considering the high incidence of rotavirus infection in children with acute diarrhea, Rotavirus screening tests seems to be necessary in children with acute diarrhea. Further study for rota virus vaccination in our country is needed.

Keywords: *Acute Diarrheal Disease; Viral Gastroenteritis; Rota Virus; Vaccine*

Abbreviations

WHO: World Health Organization; ADD: Acute diarrheal disease

Introduction

According to WHO report, 1.5 million deaths annually are due to acute diarrhea in young population [1]. Diarrheal diseases is a major cause of malnutrition in children [2]. Viral diarrhea is a major cause of morbidity in childhood and leaded to be hospital admission even in developed countries [4-6]. Although different types of viruses such as norovirus, astrovirus, adenovirus, enterovirus, parechovirus causes acute disease diseases but rotavirus is known as a common cause in pediatric group [3-8].

ADD is a common cause of hospital admission in our country [17,18].

In countries like Iran, which rotavirus vaccination in not used, knowledge of viral etiological agents of, acute diarrheal disease is so important. Rota virus is so important for strategic planning [21-22]. It might be useful for future vaccine development in the region. Shokrollahi., *et al*. showed that viral agents, especially rotavirus (48.8%), HPeV-1 (23.2%) and adenovirus (20%) are the most important causes for viral AGE in children while HBoV (8%) is infrequent during childhood. Determination of various viral pathogens of ADD is very important in planning diarrhea disease control strategies in our country where rotavirus vaccination in not routinely used [23].

Epidemiological aspects of rotavirus in children with acute diarrhea in Tehran and Ahwaz (south of Iran) had reported by some authors [24,25]. In a recent study by Talachial., *et al*. lower level for serum 25(OH) vit D in children with acute diarrhea reported [26].

Main goal of this study was to determine the incidence, clinical presentation and progression of Rota virus infection in hospitalized children with acute non bacterial diarrhea during 2 years.

Materials and Methods

This study prospective cross sectional study on 80 hospitalized children with acute non bacterial diarrhea in a third level referral hospital (Rasoulakram, Tehran, Iran) during 2 years.

This study was approved by the Ethics Committee of the Research Center of Pedi¬atric Infectious Diseases at Iran University of Medical Sciences.

Data collection was performed after obtaining parental consent.

Cases: In the first step all children with acute infectious diarrheal diseases were selected. For each case, the questionnaire was completed by an authorized physi¬cian, covering different aspects such as age, gender and other relevant demographic variables. Clinical manifes¬tations included vomiting, duration and type of diar¬rhea, duration of hospitalization and finally the lab test results (stool direct exams, biochemical parameters, complete blood count, stool culture and direct viral test in stool). The cases then underwent a thorough clinical exam.

Based on type of diarrheal, medical history, clinical symptoms and examination, stool analysis and lab results (stool exam and culture) and other lab results were selected as cases with non bacterial diarrheal diseases.

Exclusion criteria: malnutrition; chronic diarrhea, other underlying diseases (malnutrition diabetes, immune deficiency, etc), antibiotic use longer than a month, Cases with bacterial (based on stool culture) or other known causes (except viral causes) for stool direct smear (parasitic, amebic toxins, antibiotic as¬sociated diarrhea, celiac inflammatory diseases, lactase deficiency etc.) or parenteral (urinary infection, pneumo¬nia, otitis media, sinusitis etc.) were considered as non viral infectious causes and excluded from the study.

Stool samples were processed to detect rota and adenovi¬ruses. A rapid chromatographic test was performed with RFDA QUICK Rotavirus/ (R-Bio pharm, Germany, N1002) according to the manufacturer's in¬structions. At the same time, a part of the stool samples was collected on viral transport media.

Statistical analysis: The student's t test was used to determine significant in means for continuous variables. The Mann–Whitney U test and the chi-square test were used to compare groups. P-values less than 0.05 were considered statistically significant. The analyses were performed using the SPSS software (Version 11.5).

Results

The range of age in studied cases (n = 80) was between 2 - 108 month; mean age = 19.5 ± 21.2 months; 52.5% were (n = 42) male and 42.5 and (n = 38) were female. Duration of diarrhea: Mean = 6.3 ± 4.9 days. Other clinical signs in cases: Fever (T > 38) 47.5% (n = 38); Vomiting: 42.5% (n = 34); Respiratory symptoms: 16.3% (n = 16). Positive Rota virus test detected in 48.8% (n = 39) of cases with higher rate in male gender (p = 0.003); and younger age. (P = 0.03, CI = -13.4, 5.5); almost 76.9% cases aged between 1 - 18 month. The characteristic signs compared between Rotavirus positive and negative cases in Table 1. Except for severity of dehydration which was more common in positive rota virus cases (p = 0.001). No significant difference observed for other signs (fever, vomiting, Respiratory symptoms) between 2 groups.

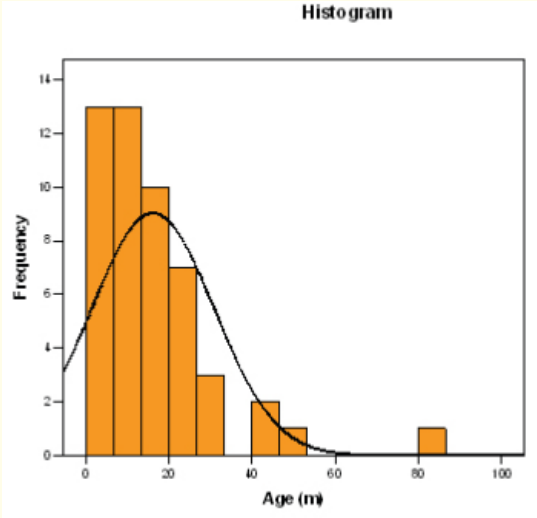

Figure 1: *Histogram of age in ADD cases.*

Clinical signs in Rota	Positive Rota virus test	Negative Rota virus test	P value
Male /female ratio	27/12	15/26	0.003
Mean age	17.49 months	21.44 months	0.03
Duration of diarrhea:	Mean = 6.3 ± 4.9 days	Mean = 6.3 ± 4.9 days	
Fever (T > 38)	53.8% (n = 21)	41% (n = 17)	0.07
Vomiting	48.7 % (n = 19)	36% (n = 15)	0.3
Respiratory symptoms	5	8	0.5
Duration of diarrhea:	Mean = 6.82 ± 5.9 days	Mean = 5.8 ± 3.7 days	0.6
Severity of dehydration	No:11 Mild: 12 Moderate:13 Severe :3	No:24 Mild:1 5 Moderate:1 Severe :1	0.001

Table 1: *Comparison the characteristic signs between Rotavirus positive and negative cases. Case group (n = 25) Control group (n = 25) p.*

Discussion

In this study upon 80 cases with acute non bacterial diarrhea during 2 years. Here we found Positive Rota virus test in stool specimen of 48.8% (n = 39) cases. Rota virus infection had the higher rate in male gender (p = 0.003); and younger age (p = 0.03). Near most cases (76.9%) were younger than 18 month. Except for severity of dehydration which was more common in positive rota virus cases (p = 0.001). No significant difference observed for other signs (fever, vomiting, Respiratory symptoms) between 2 groups.

Like here, rota virus antigen obtained from stool of ADD cases between 15 - 47% of hospitalized children with acute diarrheal disease, just in 12% of controls group. Adenovirus and astrovirus obtained from stool of Iranian children with AGE [11-21]. Saderi., *et al.* reported the incidence of enteric adenoviruses in Iranian children. 6.7% of stool specimens contained enteric adenoviruses (3.3% Ad40 and 3.4% Ad41) and 2.0% non-enteric adenoviruses [14].

Like other studies Rotavirus was the most common cause for viral AGE in near 60% of studied cases (48% single isolate and 12% coinfection with adenovirus). Adenovirus (20%); Human Boca virus (8%); coinfection Adeno and Rota (6%) diagnosed respectively. 12% was undiagnosed.

The probable viral causes might be norovirus, astrovirus or others.

The isolation rate for HBoV (6%) was significantly lower ($P < 0.0006$) than Rota; and Adenovirus ($p = 0.0001$).

This study is close to a Korean study [10]; 44.7% of all AGE cases was viral; rotavirus (25.7%), norovirus (13.7%), adenovirus (3.0%), astrovirus (1.1%), and human bocavirus (0.8%) [10].

Rotavirus is a common cause of acute gastroenteritis in Iranian children [11,14].

In Present study, 60% Rota virus positive (48% as single and 12% coinfection with adenovirus) is very close to Esteghamati., *et al.* upon 1298 stool samples with diarrhea [14], They found 59.1% positive test for rotavirus in all diarrheal diseases. 85% occurred during the first 2 years of life, and peak prevalence of severe rotavirus disease occurring from September through January. 30.9% of strains (110 positive rotavirus) G4P [8] was the most commonly detected rotavirus genotype. P[8] with G nontypeable (21.8%), G4 with P nontypeable (13.6%), G1[P8] (10.9%), and G2[P4] (5.5%) [14]. But Zamani., *et al*. reported [11] very lower rate for rotavirus antigen (15.3%). Kazemi., *et al*. [13] compared 185 hospitalized children with acute diarrhea and 91 controls; positive rotavirus antigens obtained from 30.8% of acute diarrhea and 12.1% of control children ($p < 0.05$). Hosseininasab., *et al*. reported the etiologic causes of aseptic meningitis in CSF of 65 Iranian children with by PCR, 30 (46.2%) were positive for the viruses. a virus was detected in 30 (46.2%). Non-polio human enterovirus and mumps virus were detected in 13 (43.3%) and 11 (36.7%) respectively. Mumps meningitis was found in two vaccinated and nine non-vaccinated patients [22]. Although evidence suggesting that rotavirus is a cause of central nervous system sequelae remains inconclusive [3,7]. A search of 2 large hospital discharge databases suggested that seizures are noted as part of the discharge diagnosis in the records of, at most, < 4% of patients with rotavirus diarrhea versus 7% of patients with bacterial diarrhea [3-5]. 16% of AGE in present study had neurologic manifestations (seizure: 12%; aseptic meningitis: 4%), 20% of adenoviral, 13.5% of rota virus and 33.3% of coinfection, none of Human Boca virus presented with neurologic signs but without significant differences ($P = 0.619$). Lynch., *et al.* explained 2 patients with rotavirus gastroenteritis who developed encephalopathy, rotavirus RNA was detected in the cerebrospinal fluid (CSF) by reverse transcription-polymerase chain reaction; in 1 patient, rotavirus RNA was detected on 2 occasions 3 weeks apart. Is it a true pathogen? CSF contamination that occurs at the time of lumbar puncture or in the laboratory, or carriage of rotavirus RNA in trafficking lymphocytes is another explanation [3] Nakagomi., *et al*. study Rotavirus antigen was detected in acute phase sera from 5 of 8 children with rotavirus-associated encephalopathy, confirming antigenemia However, antigen was not detected in cerebrospinal fluid, failing to provide added evidence of invasion to the brain.

Here, the adenovirus detection is higher than 2 previous Iranian studies [14,15]. Saderi., *et al*. study obtained enteric adenoviruses in 6.7% (3.3% Ad40 and 3.4% Ad41) and nonenteric adenoviruses 2.0%; from stool samples of AGE cases [14]. Modaress., *et al.* study (2004) showed adenoviruses (Ad40, 41) 2.6% of AGE cases, but not in healthy control group [15]. Hamkar., *et al.* study determined the rate of positive Rotavirus, adenovirus and astrovirus 62%, 2.3%, and 3% of samples, respectively. Astrovirus and adenovirus were detected predominantly in the 2-5-year-old age group of children, with a prevalence of 8.3% and 3.5% respectively. All studied viral gastroenteritis peaked in the winter, and minimum rate were found in summer [16].

Results of the Hamkar., *et al.* study (2006) upon 400 symptomatic cases with acute gastroenteritis in Mazandaran Province (north of Iran) showed rotavirus: 62%, adenovirus 2.3%, and astrovirus 3%. Astrovirus and adenovirus detected predominantly in the age; 2-5-yea;-and rotaviruses was in the < 1-year old age group of children [16]. In contrast to it, we found higher rate of adenovirus (20% and 12%) in AGE cases. The prevalence of astrovirus infection was estimated to be between 2 to 16% among hospitalized children with diarrhea in other countries, and 3% in Iran (Mazandran) but not studied in present study.

Although evidence suggesting that rotavirus is a cause of central nervous system squeal remains inconclusive [4-6]. Rotavirus-associated encephalopathy described by some authors. Nakagomi., *et al*. study [7] determined the rotavirus antigen in acute phase sera from 5 of 8 children with rotavirus-associated encephalopathy, confirming antigenemia, but not in cerebrospinal fluid, failing to provide added evidence of invasion to the brain [7]. There are increasing reports of cases in which patients who have seizures after an episode of rotavirus diarrhea have evidence of rotavirus in their CSF [3].

Conclusion

Considering the high incidence of rotavirus infection in children with acute diarrhea, Rotavirus screening tests seems to be necessary in children with acute diarrhea. Further studies for rota virus vaccination in our country is needed.

Acknowledgements

This study was supported by the Research Center of Pediatric Infectious Diseases affiliated by Iran University of medical sciences.

Conflict of Interest

The authors declared no conflict of interest.

Financial Disclosure

The authors declared that this study has received no financial support.

Ethical Considerations

Ethical Committee in the Research Center of Pediatric Infectious Diseases (affiliates by Iran University of Medical Sciences) has reviewed and approved the Waiver of Authorization for use of protected health information (PHI) for research purposes for the following study. Principal Investigator: Dr. Samileh Noorbakhsh, MD professor in Pediatric Infectious Diseases Department of Pediatric Infectious Diseases, Iran University of Medical Sciences.

Date of Approval: May 2011

The following PHI for which use or access is requested has been determined to be necessary for the conduct of the study.
[Insert the patient information to be used or disclosed, or attach documentation of the information.]

The use or disclosure of PHI involves no more than minimal risk.

- Granting of waiver will not adversely affect privacy rights and welfare of the individuals whose records will be used.
- The project could not practicably be conducted without a waiver.
- The project could not practicably be conducted without use of PHI.
- The privacy risks are reasonable relative to the anticipated benefits of research.
- An adequate plan to protect identifiers from improper use and disclosure is included in the research proposal.
- An adequate plan to destroy the identifiers at the earliest opportunity, or justification for retaining identifiers, is included in the research proposal.
- The project plan includes written assurances that PHI will not be re-used or disclosed for other purposes.
- Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

Bibliography

1. UNICEF/WHO. "Diarrhoes: Why children are still dying and what can be done" (2009).

2. TK Fischer., *et al*. "Hospitalizations and deaths from diarrhea and rotavirus among children <5 years of age in the United States". *Journal of Infectious Diseases* 195.8 (2007): 1117-1125.

3. Albert Z Kapikian., *et al*. "Rotavirus". In: david M. Knipe, Peter M howley. Fields virology, 4th edition. New York: Lippincott Williams and Wilkins press (2001): 1787-1834.

4. PH Dennehy. "Transmission of rotavirus and other entericpathogens in the home". *Pediatric Infectious Disease Journal* 19.10 (2000): S103-S105.

5. Centers for Disease Control and Prevention (CDC). "Reduction in rotavirus after vaccine introduction United States, 2000-2009". *Morbidity and Mortality Weekly Report* 58.41 (2009): 1146-1149.

6. Diggle L. "Rotaviros diarrhea and future prospects for prevention". *British Journal of Nursing* 16.16 (2007): 970-974.

7. Rotavirus vaccines position paper.

8. Guarino A., *et al*. "European Society for Paediatric Gastroenterology, Hepatology, and Nutrition/European Society for Paediatric Infectious Diseases evidence-based guidelines for the management of acute gastroenteritis in children in Europe". *Journal of Pediatric Gastroenterology and Nutrition* 46.2 (2008): S81.

9. Johansen K., *et al*. "Complications attributable to rotavirus-induced diarrhoea in aSwedish paediatric population: report from an 11-yearsurveillance". *Scandinavian Journal of Infectious Diseases* 40.11-12 (2008): 958.

10. Doan LT., *et al*. "Epidemiological features of rotavirus infection among hospitalized children with gastroenteristis in Ho Chi Minh City, Vietnam". *Journal of Medical Virology* 69.4 (2003): 588-594.

11. Nakagomi T., *et al*. "Incidence and burden of rotavirus gastroenteritis in Japan, as estimated from a prospective sentinel hospital study". *Journal of Infectious Diseases* 192.1 (2005): S106-S110.

12. Ray P., *et al*. "Quantitative evaluation of rotaviral antigenemia in children with acute rotaviral diarrhea". *Journal of Infectious Diseases* 194.5 (2006): 588-593.

13. Fischer TK., *et al*. "Rotavirus antigenemia in patients with acute gastroenteritis". *Journal of Infectious Diseases* 192.5 (2005): 913-919.

14. Iyadurai S., *et al*. "Benign afebrile seizures in acute gastroenteritis: is rotavirus the culprit?" *Journal of Child Neurology* 22.7 (2007): 887-890.

15. Hongou K., *et al*. "Rotavirus encephalitis mimicking afebrile benign convulsions in infants". *Pediatric Neurology* 18.4 (1998): 354-357.

16. Guarino A., *et al*. "European Society for Paediatric Gastroenterology, Hepatology, and Nutrition/European Society for Paediatric Infectious Diseases evidence-based guidelines for the management of acute gastroenteritis in children in Europe". J PediatrGastroenterolNutr2008; 46 Suppl 2:S81.

17. Saderi H., *et al*. "Incidence of enteric adenovirus gastroenteritis in Iranian children". *Journal of Clinical Virology* 24.1-2 (2002): 1-5.

18. Modarres S., *et al*. "Enteric Adenovirus Infection in Infants and Young Children With Acute Gastroenteritis In Tehran". *Acta Medica Iranica* 44.5 (2006): 349-353.

19. S Noorbakhsh., *et al*. "Neurological Manifestaions in Acute Onset of Viral Gastroentritis". *AIDS and Clinic Research* 4.1 (2013): 189.

20. S HR Monavari., *et al*. "Human *Bocavirus* in Iranian children with acute gastroenteritis". *Medical Journal of the Islamic Republic of Iran* 27.3 (2013): 127-131.

21. Kazemi A., *et al*. "The Role of Rotavirus in Acute Pediatric Diarrhea in Isfahan, Iran". *Pakistan Journal of Medical Sciences* 22.3 (2006): 282-285.

22. Eesteghamati A., *et al*. "Sentinel Hospital-Based Surveillance of Rotavirus Diarrhea in Iran". *Journal of Infectious Diseases* 200.1 (2009): S244-S247.

23. MR Shokrollahi., *et al*. "Acute Nonbacterial Gastroenteritis in Hospitalized Children: A Cross Sectional Study". *Jundishapur Journal of Microbiology* 7.12 (2014): e11840.

24. Zarnani AH., *et al*. "Role of rotaviruses in children with acute diarrhea in Tehran, Iran". *Journal of Clinical Virology* 29.3 (2004): 189-193.

25. Samarbafzadeh A., *et al*. "Epidemiological Aspects of Rotavirus Infection in Ahwaz, Iran". *Journal of Health, Population and Nutrition* 23.3 (2005): 245-249.

26. E Talachian., *et al*. "Serum levels of vitamins A and D, and zinc in children with acute diarrhea: A cross-sectional study". *Medical Journal of the Islamic Republic of Iran* 29 (2015): 207.

Volume 6 Issue 4 March 2017