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A Survey on *Rotavirus* Associated Diarrhea in 5 Main Cities of Iran

Farzaneh Jadali [1], Abdollah Karimi [2*], Fatemeh Fallah [3], Mohsen Zahraei [4], Abdolreza Esteghamati [4], Masoumeh Navidinia [3], Saadat Adabian [3]

[1] Department of Pediatric Pathology, Pediatric Infections Research Center (PIRC), Mofid Children Hospital, Shahid Beheshti University of Medical Sciences, Tehran, IR Iran

[2] Pediatric Infections Research Center (PIRC), Mofid Children Hospital, Shahid Beheshti University of Medical Sciences, Tehran, IR Iran

[3] Department of Medical Microbiology, Pediatric Infections Research Center (PIRC), Mofid Children Hospital, Shahid Beheshti University of Medical Sciences, Tehran, IR Iran

[4] Department of Pediatric Infectious Disease, Faculty of Medical Science, Tehran University of Medical Sciences, Tehran, IR Iran

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ABSTRACT

Background: *Rotaviruses* a major group of viruses that cause severe gastroenteritis in young children worldwide. Many different viruses can cause gastroenteritis, including *Noroviruses, Adenoviruses, Sapoviruses,* and *Astroviruses*. Serum antibody studies show that most of the children are infected with *Rotavirus* at least once in their life by the age of 3. In the world, approximately 400-600 thousand children in poor countries die annually by *Rotavirus*-associated dehydration. Most of the deaths occur in these countries because of delay in treatment. Despite low death rates in industrialized countries, good hygiene and sanitation do not appear to reduce the prevalence or prevent the spread of *Rotavirus*.

Objectives: This study was aimed to detect *Rotavirus* in stool samples of infected patients using enzyme-linked immunosorbent assay (ELISA) serological method in 5 cities of Iran.

Materials and Methods: In this descriptive study, 2988 stool samples of patients with acute gastroenteritis were collected from children's hospitals of 5 main cities of Iran. The samples were sent in frozen condition to pediatric infection research center in Tehran and stored at -70°C. ELISA test was performed for detection of *Rotavirus* antigens. The mean age of study population was 1 to 5 years.

Results: ELISA method on 2988 stool samples from 5 cities revealed rotavirus-positive results in 55.48% cases, including 8.97% in Tehran, 7.56% in Tabriz, 7.76% in Mashhad, 14.42% in Shiraz, and 16.77% in Bandar Abbas). 59.2% of positive samples occurred in males and 40.8% in females.

Conclusions: Rotavirus is one of the major causes of gastroenteritis in children in Iran that can be easily detectable by ELISA method through which early diagnosis, treatment, and preventive vaccination can dramatically reduce mortality and morbidity rates of the disease.

▸ *Implication for health policy/practice/research/medical education:*

Rotavirus the most common cause of diarrhea in children and due to it's high morbidity a specific medication, Nowadays vaccination prevention is highly recommended.

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* *Corresponding author:* Abdollah Karimi, Pediatric Infections Research Center, Department of Pediatric Infectious Diseases, Mofid Children Hospital, Shariati St, Tehran, IR Iran. Tel: +98-9123951537, Fax: +98-22229641, *E-mail:* dr_akarimi@yahoo.com

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1. Background

Gastroenteritis means the inflammation of stomach, small and large intestines. *Rotavirus* is the most common cause of severe gastroenteritis among children worldwide. Severe gastroenteritis results in approximately 800,000 deaths (1) annually by some bacteria (i.e. *Staphylococcus aureus* (2), *Escherichia coli* (3), *Clostridium difficile*, *Yersinia enterocolitica*, *Salmonella, Shigella* (4), *Campylobacter* (5), parasites (such as *Giardia*, *Cryptosporidium*) (6), and viruses. Some viruses causing gastroenteritis include *Noroviruses*, *Adenoviruses*, *Sapoviruses*, human *Caliciviruses,* and *Astroviruses* (7-9). Serum antibody studies show that likely all children have been infected with *Rotavirus* at least once in their life by the age of 3.

Rotaviruses are ubiquitous; 95% of children worldwide are infected by the age of 3 to 5. Theinfection is frequently asymptomatic caused by unusual strains of rotaviruses. The disease is most prevalent between ages 4 and36 months in children and sometimes occurs severely thatrequires hospitalization. *Rotavirus* infection in adults is usually subclinical but occasionally causes more severe clinical picture in parents of children with *Rotavirus* diarrhea, immune-compromised patients (including those with HIV), old individuals, and travelers to developing countries. In temperate climates, *Rotavirus* diarrhea occurs predominantly during the fall and winter; in tropical settings and in developing countries, seasonality is less marked.

Rotaviruses are shed in large numbers during episodes of diarrhea, and usually are detectable by antigen enzyme immunoassays (EIA) up to 1 week after infection or for more than 30 days in immune-compromised patients. The predominant mode of *Rotavirus* transmission is fecal-oral. Spread of the virus through respiratory secretions, person-to-person contact, or contaminated environmental surfaces has also been speculated because of high rates of infection in the first 3 years of life regardless of sanitary conditions, failure to document fecal-oral transmission in several outbreaks of *Rotavirus* diarrhea, and dramatic spread of rotavirus over large geographic areas in winter. Animal-to-human transmission does not appear to be common, although human rotavirus strains that possess a high degree of genetic homology with animal strains have been identified (10).

In the world, approximately 400-600 thousand children in poor countries die annually by *Rotavirus*-associated dehydration. Most of the deaths occur in these countries due to delay in treatment. Despite of low death rates in industrialized countries, good hygiene and sanitation do not appear to reduce the prevalence or prevent the spread of *Rotavirus*. *Rotavirus* particles are 65-75 nanometers in diameter, with a double protein shell and 11 unique strands of double-stranded RNA. The majority of *Rotaviruses* known to infect humans and animals share a common-group antigen and are termed group A *Rotaviruses* (11). *Rotavirus* gastroenteritis is manifested by some main symptoms such as abdominal pain, fever, diarrhea, lethargy, and vomiting that may lead to hypovolemic shock and dehydration (12). Diarrhea is the second most common cause of childhood mortality worldwide, estimated to be responsible for 1.76 million deaths annually between 2000 and 2003 and 1.87 million deaths in children under the age of 5 years in 2004 (13-15). *Rotavirus* can infect all children by the age of five regardless of socioeconomic status or environmental conditions (16). The world health organization (WHO) estimates that 527,000 childhood deaths are caused by *Rotavirus* disease each year (17). In developing countries, *Rotavirus* is the most common cause of childhood mortality due to severe diarrhea (18) *Rotaviruses* are the most common agents associated with benign seizures (19). A study in Iran reported 59.1% *Rotavirus*-positive cases among children with acute gastroenteritis (20). The most dominant virus, group A, causes diarrheal diseases worldwide.

2. Objectives

This study was aimed to determine the prevalence of *Rotavirus* gastroenteritis in children under five years old with acute gastroenteritis using ELISA, a cheap and fast method, on 2988 samples, for detection of the virus by age, sex, and situation in 5 cities of Iran (21).

3. Materials and Methods

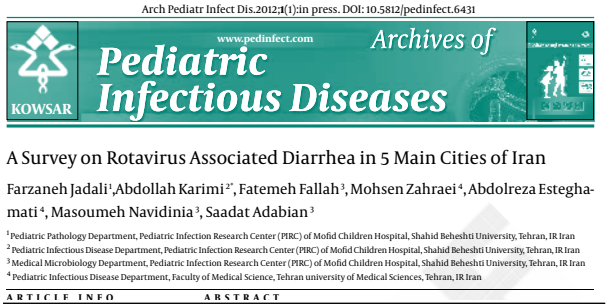
Stool specimens (n = 2988) were collected from patients under five years old with acute diarrhea hospitalized in Tehran, Shiraz, Tabriz, Bandar Abbas, and Mashhad, and referred to pediatric infection research center (PIRC) of Mofid children's hospital in freezed condition during April 2010 to March 2011 and stored at minus 70°C. The cases were identified by reviewing hospital admission records of demographic characteristics and symptoms of patients.

A commercially available ELISA kit (Rotaclone; Meridian Bioscience Inc., Cincinnati, OH) was used to detect group A *Rotavirus* antigen. (IDEIA *Rotavirus*, Dakocytomation Ltd. Denmark House, Angel Drove, Ely, cambsCB7 4ET, UK, Lot: 212985 kit). Results were read by an ELISA plate reader with the filters set at 450 nm and 620-650 nm. Controls were included each time the kit was run.

4. Results

Fecal specimens from 2988 children below 5 years old with acute diarrhea hospitalized in 5 cities of Iran (Tehran, Shiraz, Tabriz, Bandar Abbas, Mashhad) from April 2010 to March 2011 were examined in PIRC of Mofid children's hospital, Tehran/Iran to know the prevalence of *Rotavirus* diarrhea from different locations of Iran using double antibody sandwich ELISA analysis. The prevalence of *Rotavirus* was the highest in Bandar Abbas (16.77%) and

Shiraz (14.42%), *Rotavirus* and the least in Tabriz (7.56%). Stool samples were positive for *Rotavirus* in 55.48% of cases (*Figure 1*). There was 59.9% of samples from male patients and 40.1% from females. *Rotavirus* diarrhea was significantly high ($P < 0.01$) in children between 11 to 20 months (43.28%). Children from families of middle socioeconomic status (69.35%) mostly suffered from the disease ($P < 0.001$). Peak incidence of rotavirus diarrhea was in winter (41.26%) and showed inverse relation to temperature, humidity, and rainfall. Besides diarrhea, vomiting was a significant clinical manifestation.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[1] Pediatric Pathology Department, Pediatric Infection Research Center (PIRC) of Mofid Children Hospital, Shahid Beheshti University, Tehran, IR Iran
[2] Pediatric Infectious Disease Department, Pediatric Infection Research Center (PIRC) of Mofid Children Hospital, Shahid Beheshti University, Tehran, IR Iran
[3] Medical Microbiology Department, Pediatric Infection Research Center (PIRC) of Mofid Children Hospital, Shahid Beheshti University, Tehran, IR Iran
[4] Pediatric Infectious Disease Department, Faculty of Medical Science, Tehran university of Medical Sciences, Tehran, IR Iran

ARTICLE INFO ABSTRACT

Figure 1. The Prevalence of *Rotavirusin* 5 Cities of Iran by ELISA Method

5. Discussion

Control of *Rotavirus* through improvements in hygiene and sanitation is difficult since this virus often transmits from person to person easily and therefore, the proportion of diarrhea deaths attributed to *Rotavirus* may increase. Eighty two percent of rotavirus deaths occur among children in undeveloped countries (22). In a study conducted in Ýzmir, Turkey, the reports showed that *Rotavirus* among children less than five years old is the most commonly detected etiologic agent responsible for 39.8% of acute gastroenteritis admissions (23). Another study in Iran showed 59.1% *Rotavirus*-positive cases among 2198 children aged 5 years with acute gastroenteritis (24) that agreed with this study in which the prevalence was 55.48 % (20). In other countries, the prevalence rates for *Rotavirus*-positive cases were reported as follows: Pakistan, 13.7%; England, 43% (25); Vietnam, 50% (26); Poland, 41 % (27): and Kuwait, 45% (28). Of 260 children with acute diarrhea in Erbil, Iraq, 96 patients (37%) were infected with *Rotavirus* (29).

In a pilot study conducted by Román in 2005, 100 stool samples from patients with gastroenteritis were examined to determine the presence of *Rotavirus* using immunoassays and molecular diagnostic methods; the result was 11 *Rotavirus*-positive samples. Using reverse transcriptase-polymerase chain reaction (RT/PCR) method resulted in detection of 51 *rotavirus*-positive samples. These results substantiated the generally accepted concept that molecular techniques were more sensitive than serological diagnostic tests. In addition, these data suggest that *Rotavirus* is an important etiologic agent for gastroenteritis in local pediatric population (30).

Rotavirus gastroenteritis occurred in males and females. In a study performed in Iran, the *Rotavirus* diarrhea in females less than five years old (18.0%) was higher than that was detected in 187 (19%) specimens tested by ELISA. *Rotavirus* was detected in 158 (28%) out of 561 specimens collected from hospitalized children, whereas it was detected in only 29 (7%) out of 423 children treated in oral rehydration unit (outpatients). Distribution of affected children less than 5 years old showed that 159 cases (83%) occurred among children aged between 4 and 23 months, whereas only 8 cases (4.3%) occurred in the first 3 months of life (31). In our study the distribution of *Rotavirus* occurred among children less than 2 years old (63%).

In another study performed in Iran, the *Rotavirus* diarrhea in females less than five years old (18.0%) was higher than that in males (13.7%) of the same age (32) but our study and the other study showed different results with no relationship between *Rotavirus* infection and sex. Seasonality is obvious for *Rotavirus* infection so that majority of cases in temperate climates occur in winter months between November and February (33).

A multicenter study in 5 developing countries including Pakistan conducted by WHO CDD program revealed that only 1.8% of cases were presented with severe dehydration and these were mostly due to *Rotaviruses*; in the study all methods detected *Rotavirus* to varying degrees but ELISA was found to be the most sensitive method with 72.4% stools being positive (34).

In 2005, *Rotavirus* was detected in 48 patients (10%) in Saudi Arabia using latex agglutination test. ELISA detected 46/48 positive samples. Ten negative samples with latex test were also negative with ELISA. Infection with *Rotavirus* was more frequent among infants and children < 2 years old, with a maximum incidence among children 0-12 months. The prevalence of *Rotavirus* infection in Saudi nationals was 3.1% compared to 6.9% in other nationalities (35).

Since the time of study was limited to 1 year, consideration of *Rotavirus* genotyping to detect the most prevalence genotypes for vaccination is necessary. In near future, continuous and broader surveillances on circular *Rotavirus* strains are required in Iran. Also, there is a great need for defining the prevalence of *Rotavirus*-associated disease burden and strain in Iran. We also need to conduct *Rotavirus* vaccine trials to assess its efficacy and safety in our settings. In addition, our data suggest that rotavirus is an important etiologic agent of gastroenteritis in local pediatric population. More extensive studies are necessary to determine the prevalence of *Rotavirus* in Iran in order to design effective control measures and protect our population against this pathogen. Agreement with study in 2003 by Phukan AC revealed that 23.27% of patients were affected by *Rotavirus*. *Rotavirus* diarrhea was significantly high in children under 2 years old (37.75%) (36).

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Authors' Contribution

None declared.

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