

## Original Research Article

# Rapid Diagnosis of Rota-Adenoviruses for Acute Gastroenteritis in hospitalized Children under 4 Years Old, Baghdad

Razaq Hadi Eissa Al-Sayidi<sup>1</sup>, Hula Y.Fadhil<sup>2\*</sup>, Faisal G.AL- Hamdani<sup>1</sup>

<sup>1</sup>Department of Virology, The National Central Public Health Laboratory (NPL), Ministry of Health, Baghdad-Al-Andlus Street, Iraq

<sup>2</sup>Department of Biology, College of Science, University of Baghdad, Baghdad-Al-Jadiria, Iraq

\*Corresponding author

## ABSTRACT

### Keywords

Rotavirus;  
Enteric  
Adenovirus;  
Gastroenteritis;  
Immuno-  
chromotography  
and Iraqi  
children.

Rotavirus and adenovirus are respectively the first and second most common agents responsible for acute gastroenteritis, mainly in young children. In Iraq, little data are recorded about these viral infections other than Baghdad province, so we designed this study to investigate the prevalence frequencies of both viruses and their role in viral diarrheal. Out of 450 diarrhea cases, 150 stools sampled have negative tests for parasites and bacterial infections were targeted in this study. Frequency of rotavirus and adenovirus were observed in 25.5% of all children with acute gastroenteritis, while the distribution of positive cases for rotavirus was 91.3%, 2.6% for adenovirus and 6.09% for rota-adenoviruses among studied groups. Significant frequency showed in children less than 2 years of each rota and rota-adenoviruses, whereas the adenovirus in children with 3-4 years. The highest prevalence of rotavirus among viral pathogens in children with diarrhea, we recommended more studies are necessary in order to evaluate the vaccine efficiency. Moreover, these findings established the evidence that adenovirus play a major role in coinfection with rotavirus and severity of diarrhea among children especially less than 3 years old.

## Introduction

Acute gastroenteritis is one of the most common diseases in humans worldwide. Viral gastroenteritis is a global problem in infants and young children (Magalhaes et al., 2007). Diarrhea remains the second leading cause of death around the world for children under 5 years of age (Black et al., 2010). In the developing world rotavirus may account for 1 million

childhood deaths as well as significant morbidity each year (Kane et al., 2004).

Rotavirus from group A is the more prevalent cause of viral gastroenteritis and can be detected by a variety of techniques including latex agglutination (LA) and enzyme immunoassay (EIA). The enteric serotypes that are most frequently

associated with gastroenteritis caused by adenovirus are 40 and 41, which belong to subgenus A and serotypes 1, 2, 5, and 6 of subgenus C have been involved in the etiology of acute diarrhea (Baum 2000). Adenoviruses are second only to rotavirus as the most important causative agents of acute infantile gastroenteritis (Zlateva et al., 2005).

The main symptoms of rotavirus gastroenteritis (RVGE) are fever; abdominal pain, lethargy; diarrhea and vomiting that may lead to hypovolemic shock and dehydration. Severe cases may lead to death. The World Health Organization (WHO) estimates that 527,000 children under the age of five years die of rotavirus disease each year. Children in the poorest countries account for 82% of rotavirus deaths (Khoury et al., 2011). The fact that enteric adenoviruses produced symptoms that were milder than symptoms in patients with rotavirus infection may have resulted in under-reporting (Hamkar et al., 2010).

In Iraq, the death rate in children <5 years of age was reported to be 130/1,000 for boys and 120/1,000 for girls in 2003 (World Health Organization, 2003). Diarrhea is a major cause of illness and death in Iraqi children. Furthermore, little data is recorded about these viral infections other than Baghdad province, so we designed this study to investigate the prevalence frequencies of both viruses and their role in viral diarrheal.

## **Materials and Methods**

### **Stool Sample**

A total of four hundred and fifty hospitalized children under 4-years, who suffering from acute gastroenteritis were tested for common bacteria and parasites.

Out of 450 diarrhea cases, 150 stools sampled have negative tests for parasites and bacterial infections were targeted in this study. The clinical history, socio-demographic characteristics, physical examination and laboratory tests were recorded. Stool samples were collected between January to March 2013 and stored at -20°C for use.

### **Identification of Rota and Adenoviruses**

Immuno-chromatography test (ICT) was used for rotavirus and adenovirus antigen detection. Further, all selected samples were analyzed for group A rotavirus using latex (Barcelona-Spain) and ELISA (ProSpect™ Oxoid Ltd, UK) as a confirmatory test. VIKIA rota-adenoviruses (bioMérieux, France) are a rapid test for the qualitative dual detection of rotavirus and adenovirus in human stool. This test uses immunological reactions performed on a test strip by migration (ICT or lateral flow format) according to manufacturer's instructions.

### **Statistical Analysis**

The data and graphs were carried out using spss program version 20 IBM. The proportion and their frequencies were checked by applying chi-square test to estimate the relative risk of rota-adenoviruses to diarrheal infection. The P-values < 0.05 considered statistically significant.

## **Results and Discussion**

Our finding observed that the frequency of rotavirus and adenovirus were 25.5% of all children with acute gastroenteritis, while it represented as 76.7% of children who had negative testing for bacteria and parasites (Table 1). On the other hand, the

distribution of positive cases for rotavirus was 91.3%, 2.6% for adenovirus and 6.09% for rota-adenoviruses among studied groups. A significant incidence of study viral infections among diarrhea cases in children were appeared ( $P < 0.001$ ).

According to the age groups, the highest frequency showed in children less than 2 years of each rota and rota-adenoviruses, whereas the adenovirus in children with 3-4 years. The significant rotavirus infection was shown in all age groups ( $P < 0.05$ ). Moreover, the highest significant rota and rota-adenoviruses infection were noticed in children with less than 2 years ( $P < 0.001$ ) (Fig. 1). Regarding the adenovirus infection was showing significant in children with 3-4 years ( $P < 0.001$ ). In the current study, we reported that male children more exposure to viral infection than female and there is significant differences between them ( $P < 0.05$ ).

Figure 2 demonstrates that infected children with rota-adenovirus more sever of clinical signs than single infection with these viruses, although there are no significant differences between the severity of symptoms and the type of viral infection ( $P = 0.06$ ).

In several international reports, it was evident that viral pathogens are the most common cause of gastroenteritis in developing countries Worldwide (Mertus et al., 1990; McIver et al., 2001; Simpson et al., 2007). Our study showed a rotavirus prevalence of 24.89% in children with diarrhea. Similar value was obtained previous study in Rondonia (Magalhes et al., 2007), this comparison may be due to studied sample size. Meanwhile, several Iraqi investigators listed the rotavirus

frequencies among diarrhea cases between 14.9% and 56% (Hussien and Hassan, 2000; Ahmed et al., 2006; Al-Marzoqi et al., 2011; Zaman et al., 2012; Al-Khafaj and Al-Jiboury, 2013).

Not many studies on adenovirus detection in children with diarrhea have been carried out. Thus, our findings indicated that the adenovirus prevalence of 2.23% in children with acute gastroenteritis as causal or coinfection with rotavirus. This observation differs from both Iraqi studies that reported 6.6% and 20% of children with acute gastroenteritis as enteric adenovirus infection in Babylon and Kirkuk provinces, there is no reported coinfection with rotaviruses (Al-Marzoqi et al., 2011; Zaman et al., 2012), but it was agreed with other previous studies in developing countries such as in Iran, China, Singapore and Indonesia showed that enteric adenovirus was found in 2.3%, 2.5%, 3% and 4% of diarrheal patients respectively (Hamkar et al., 2010; Subekti et al., 2002; Qiao et al., 1999; Mendis et al., 1995).

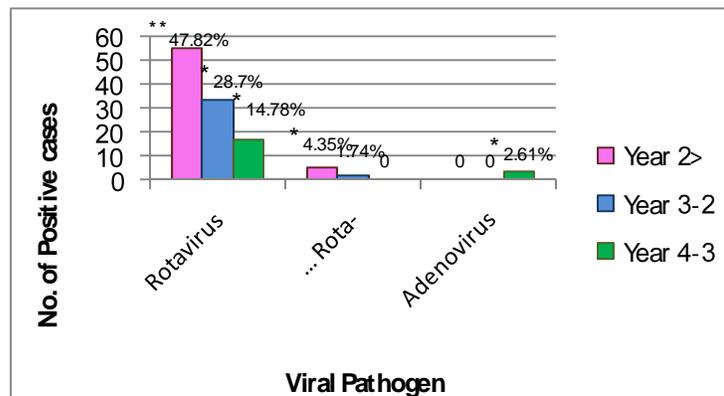
As mentioned above, rotavirus and adenovirus were caused 91.1% and 6.8% of viral pathogens in selected children with diarrhea, respectively. These prevalences are different from those detected in our population. In the current study, immunochromatography test was established that higher (100%) sensitivity and specificity by detecting of rotavirus with latex and ELISA assays.

This finding indicated that 23.3% was absent for common bacteria, parasites and viruses causes diarrhea. This percent may be explained many causes like other viruses, medications (such as antibiotics), lactose intolerance and artificial sweeteners.

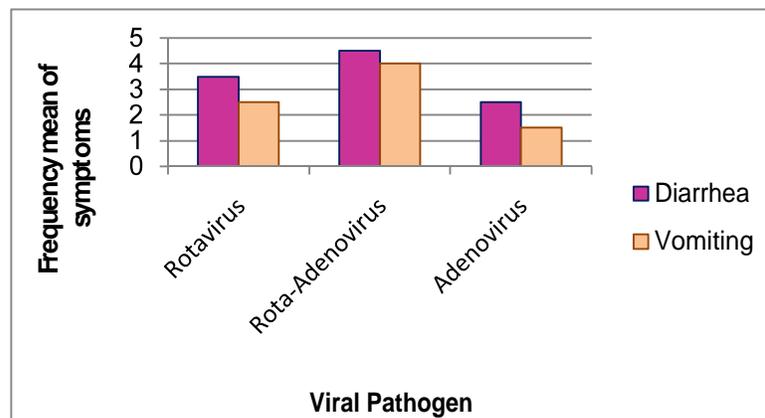
**Table.1** Distribution of positive cases and their frequency for Rota and Adenoviruses among children with diarrheal infection

Viral pathogen (no. of positive)	Frequency among diarrhea cases		
	Total diarrhea cases, n=450	Only negative cases for bacteria and parasites, n=150	Only Positive cases for Rota and Adenovirus, n=115
Rotavirus (105)	23.33%	70%	91.3%
Adenovirus (3)	0.67%	2%	2.61%
Rota-Adenovirus (7)	1.56%	4.7%	6.09%
Total (115)	25.56%	76.7%	100%

**Fig.1** Proportion of viral infection by age groups among 150 children suffering of gastroenteritis after testing for bacteria and parasites, between Januarys to March 2013. The asterisk indicates that the differences are significant. \* P<0.05; \*\*P<0.001.



**Fig.2** Observation of clinical symptoms according to viral infection among study group, no significant differences between the severity of symptoms and the type of viral infection (P=0.06).



Generally, rotavirus diarrhea is more likely to be associated with fever, vomiting, and dehydration than diarrhea caused by other pathogens (Seo and Sim, 2000). In our study, fever, vomiting, and dehydration were observed at severity in the children infected with rota-adenoviruses. These symptoms did not differ significantly from those with single viral infection in children, indicating the role of adenovirus as coinfection in diarrheal disease in Iraqi children. Furthermore, the coinfections could cause difficulties for pediatricians and health care workers in terms of the diagnosis, treatment, and prophylaxis of diarrhea in children (Vu Nguyen et al., 2004).

This study observed the significant appearance of rotavirus infection in all age groups and highly significant in children less than 2 years were seen, whereas adenovirus was distributed among aged children either singly or coinfection. Adenovirus can be seen as an etiologic agent among all age groups (Giordano et al., 2001; Cam and Gumus, 2003; Topkaya et al., 2006). A study by Vu Nguyen et al (2004) that detected rotavirus at the highest rate among the children in all age groups those with all three symptoms. However, in developing countries the peak rates occur in the second year of life. This could lead to the beneficial application of rotavirus vaccine to children in our country since 2013. On the other hand, this might partly be explained by the fact that older children acquired protective immunity during previous exposures to rotavirus and are therefore more resistant to infection with this agent (Jiang et al., 2002; Staat et al., 2002). The highest prevalence of rotavirus among viral pathogens in children with diarrhea, we recommended more studies are necessary in order to evaluate the vaccine efficiency. Moreover, these findings established the evidence that adenovirus

play a major role in coinfection with rotavirus and severity of diarrhea among children especially less than 3 years old.

## References

- Ahmed, H.M., Brian, J., Coulter, S., Nakagomi, O., Hart, C.A., Zaki, J.M., Al-Rabaty, A.A., Dove, and Cunliffe, W.A. 2006. Molecular Characterization of Rotavirus Gastroenteritis Strains, Iraqi Kurdistan. *Emerging Infectious Diseases*. 12 (5):824-26.
- AL- Khafaji, Y.A. and AL-Jiboury, H.J. 2013. Detection of Rotavirus in diarrhea stool samples of children with acute gastroenteritis in Babylon governorate, Iraq. *International Research Journal of Microbiology*. 4(3):84-88.
- Al-Marzoqi, A.H., Shemmran, A.R. and Al-Nafee', M.K. 2011. Role of Rotavirus and Adenovirus in Acute Infantile Gastroenteritis in Infants younger than one year of age in Babylon Province. *University of Babylon Repository : Research papers and academic*. 11:1-7.
- Baum SG 2000. Adenovirus. In GL Mandell, JE Bennet, R Dolin, *Principles and Practice of Infectious Diseases*, Churchill Livingstone, New York, p. 1624-1630.
- Black, R.E., Cousens, S., Johnson, H.L., Lawn, J.E., Rudan, I., Bassani, D.G., Jha, P., Campbell, H., Walker, C.F., Cibulskis R, et al. 2010. Global, regional, and national causes of child mortality in 2008: a systematic analysis. *Lancet*. 375(9730):1969–1987.
- Cam, H. and Gumus, A. 2003. Rotavirus incidence in cases with acute gastroenteritis. *HipokratPediatriDergis* i. 3: 127-130.
- Giordano, O.M., Ferreyra, J.L. and Isa, B.M. 2001. The epidemiology of acute viral gastroenteritis in hospitalized children in Cordoba City, Argentina: An Insight of Disease Burden. *Rev Inst Med Trop*. 43: 193-197.
- Hamkar, R., Yahyapour, R., Noroozi, M., Nourijelyani, K., Jalilvand, S., Adibi, L., Vaziri, S., Poor-Babaei, A.A., Pakfetrat, A.

- and Savad-Koochi, R. 2010. Prevalence of Rotavirus, Adenovirus, and Astrovirus Infections among Patients with Acute Gastroenteritis in Northern Iran. *Iranian J Publ Health*. 39(2):45-51.
- Hussein, A.M. and Hassan, M.K. 2000. Rotavirus Infection Among Hospitalized Children with Acute Watery Diarrhea In Basrah – Iraq. *Bahrain Medical Bulletin*. 22 (4):1-6.
- Jiang, B., J. R. Gentsch, and R. I. Glass. 2002. The role of serum antibodies in the protection against rotavirus disease: an overview. *Clin. Infect. Dis*. 34:1351–1361.
- Kane, E.M., Turcios, R.M., Arvay, M.L., Garcia, S., Bresee, J.S. and Glass, R.I. 2004. The epidemiology of rotavirus diarrhea in Latin America. Anticipating rotavirus vaccines. *Rev Panam Salud Publica*. 16:371–377.
- Khoury, *et al.* 2011. Burden of rotavirus gastroenteritis in the Middle Eastern and North African pediatric population. *BMC Infectious Diseases*. 11:9.
- Magalhaes, G.F., Nogueira, P.A., Grava, A.F., Penati, M., Pereira da Silva, L.H. and Orlandi, P.P. 2007. Rotavirus and adenovirus in Rondônia. *Mem Inst Oswaldo Cruz, Rio de Janeiro*. 102(5): 555-557.
- McIver, C.J., Hansman, G., White, P., Doultree, J.C., Catton, M. and Rawlinson, W.D. 2001. Diagnosis of enteric pathogens in children with gastroenteritis. *Pathology*. 33:353–358.
- Mendis, L., Kumarasinghe, G., Chow, C., Liew, H.Y., Ramachandran, N.P., Yayawardane K *et al.* 1995. Bacteria, viruses, yeasts and protozoans associated with diarrheal disease in Singapore. *Pathology*. 27: 48-52.
- Mertens, T.E., Wijenayake, R., Pinto, M.R., Peiris, J.S., Wijesundera, M.D., Eriyagama, N.B., Karunaratne, K.G. and Ranaweera, L.R. 1990. Microbiological agents associated with childhood diarrhea in the dry zone of Sri Lanka. *Trop Med Parasitol*. 41(1):115–120.
- Qiao, H., Nilsson, M., Abreu, E.R., Hedlund, K.O. and Johansen, K. 1999. Viral diarrhea in children in Beijing, China. *J Med Virol*. 57:390-6.
- Seo, J. K., and J. G. Sim. 2000. Overview of rotavirus infections in Korea. *Pediatr. Int*. 42:406–410.
- Simpson, R., Aliyu, S., Iturriza-Gomara, M., Desselberger, U. and Gray, J. 2007. Infantile viral gastroenteritis: on the way to closing the diagnostic gap. *J Med Virol*. 70:258–262.
- Staat, M. A., P. H. Azimi, T. Berke, N. Roberts, D. I. Bernstein, R. L. Ward, L. K. Pickering, and D. O. Matson. 2002. Clinical presentations of rotavirus infection among hospitalized children. *Pediatr. Infect. Dis. J*. 21:221–227.
- Subekti, D., Lesmana, M., Tjaniadi, P., Safari, N., Frazier, E., Simanjuntak C, *et al.* (2002). Incidence of Norwalk-like viruses, rotavirus and adenovirus infection in patients with acute gastroenteritis in Jakarta, Indonesia. *FEMS Immunol Med Microbiol*. 33: 27-33.
- Topkaya, A.E., Aksungar, B., Özakkafl, F. and Çapan, N. 2006. Examination of rotavirus and enteric adenovirus in children with acute gastroenteritis. *Türk Mikrobiyol Cem Derg*. 36 (4): 210-213.
- Vu Nguyen, T., Le Van, P., Le Huy, C. and Weintraub, A. 2004. Diarrhea Caused by Rotavirus in Children Less than 5 Years of Age in Hanoi, Vietnam. *J. Clin. Microbiol*. 42(12): 5745–5750.
- World Health Organization (2003). Iraq. Statistics by country or region. [cited 2005 Oct 19]. Available from <http://www3.who.int/whosis/country/indicators.cfm?Country=IRQ&language=English>
- Zaman, N.A., Al-Tae, A.A. and Saadoon, I.H. 2012. Prevalence of Rotavirus, Adenovirus, and Rotavirus denovirus Coinfection among children less than 5 years in Kirkuk city. Second Scientific Conference – Science College – Tikrit University. 116-120.
- Zlateva, K.T., Maes, P., Rahman, M. and Van Ranst, M. 2005. Chromatography paper strip sampling of enteric adenoviruses type 40 and 41 positive stool specimens. *Virol J*. 2:6–10.