Acute norovirus gastroenteritis in up to five years children highly rotavirusvaccinated population in southern Brazil

Gastroenterite aguda de norovírus em crianças de até cinco anos altamente vacinadas com rotavírus no sul do Brasil

Gastroenteritis aguda por norovirus en niños de hasta cinco años altamente vacunados por rotavirus en el sur de Brasil

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Amanda Razera

ORCID: https://orcid.org/0000-0002-7167-8885 Universidade Estadual do Centro-Oeste, Brazil E-mail: amanda.razera97@gmail.com

Leni Macedo Semaan

ORCID: https://orcid.org/0000-0002-4475-2429 Universidade Estadual do Centro-Oeste, Brazil E-mail: l.m.semaan@gmail.com

Veronica Aparecida Ambrosini

ORCID: https://orcid.org/0000-0002-6754-4147 Universidade Estadual do Centro-Oeste, Brazil E-mail: veronika_ambrosini@hotmail.com

Jean Rodrigo Santos

ORCID: https://orcid.org/0000-0002-6112-5611 Universidade Estadual do Centro-Oeste, Brazil E-mail: rodrigosantosjean105@gmail.com

Emerson Carraro

ORCID: https://orcid.org/0000-0001-5420-2300 Universidade Estadual do Centro-Oeste, Brazil E-mail: emersoncarraro@bol.com.br

Abstract

The acute gastroenteritis remains a problem social, economic and of the public health of the global impact and among the main causative agents are the viruses. This study aimed to show the circulation of rotavirus (RoV) and norovirus (NoV) infections in children under 5 years, vaccinated or not against RoV, enrolled in the health system presented gastroenteritis. From March 2011 to February 2012 a total of 160 stool samples were collected, overall positivity rates were 11.9% (19/160) for NoV and was not found infected patients with RV. The children include had a mean of 2.8 and a median of 3 years of old, and the average of rotavirus vaccination rate was 83.85%. This result shows that this circulating NoV and suggests a reduction in the occurrence of RoV infection in children with high vaccination coverage rate.

Keywords: Rotavirus; Norovirus; Gastroenteritis.

Resumo

A gastroenterite aguda continua sendo um problema social, econômico e de saúde pública do impacto global e entre os principais agentes causadores estão os vírus. Este estudo teve como objetivo mostrar que a circulação de infecções por rotavírus (Rov) e norovírus (Nov) em crianças menores de 5 anos, vacinadas ou não contra Rov, matriculadas no sistema de saúde apresentavam gastroenterite. De março de 2011 a fevereiro de 2012 foram coletadas 160 amostras de fezes, as taxas de positividade geral foram de 11,9% (19/160) para Nov e não foram encontrados pacientes infectados com VD. As crianças incluídas tiveram média de 2,8 e mediana de 3 anos, e a média de vacinação contra rotavírus foi de 83,85%. Esse resultado mostra que esse Nov circulante sugere redução na ocorrência de infecção por Rov em crianças com alta cobertura vacinal.

Palavras-chave: Rotavírus; Norovírus; Gastroenterite.

Resumen

La gastroenteritis aguda sigue siendo un problema social, económico y de salud pública del impacto global y entre los principales agentes causantes se encuentran los virus. Este estudio tuvo como objetivo mostrar la circulación de infecciones por rotavirus (RoV) y norovirus (NoV) en niños menores de 5 años, vacunados o no contra RoV, inscritos en el sistema de salud presentaron gastroenteritis. De marzo de 2011 a febrero de 2012 se recogieron un total de 160

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muestras de heces, las tasas generales de positividad fueron del 11,9% (19/160) para NoV y no se encontraron pacientes infectados con VD. Los niños incluidos tuvieron una media de 2,8 y una mediana de 3 años de edad, y el promedio de la tasa de vacunación por rotavirus fue del 83,85%. Este resultado muestra que este NoV circulante y sugiere una reducción en la incidencia de la infección por RoV en niños con alta tasa de cobertura de vacunación.

Palabras clave: Rotavirus; Norovirus; Gastroenteritis.

1. Introduction

Due to its economic and social impact, viral gastroenteritis continues to be an important public health problem, being caused mainly by rotavirus (Rov) and norovirus (Nov) (Bányai et al., 2018).

With the introduction of vaccination against Rov in immunization programmer the mortality generated by diarrhea decreased significantly, as in 2010 it was estimated at 1,24 million deaths among children under 5 years of age and in 2013 this estimate was updated to 752000 deaths. Its incubation period is short, usually less than 48 hours and the clinical manifestations of the infection vary and depend on whether it is the first infection or reinfection (Tate et al., 2016; Cdc, 2021).

Rov was reported as the main agent of viral gastroenteritis in childhood in Brazil, however, after the beginning of vaccination, the epidemiology of acute gastroenteritis (AGE) was modified, and recent studies have pointed to Nov as one of the main etiological agents (Kamioka et al., 2019; Sarmento et al., 2021).

Worldwide, estimated Nov to be responsible for one-fifth of all AGE cases, leading to an expenditure of approximately \$4.2 billion per year to health care systems and over 200,000 deaths, primarily in low- and middle-income countries (Lopman et al., 2016; Ahmed et al., 2014; Atmar et al., 2018; Bányai et al., 2018). In the case of norovirus infection, the incubation period can vary from 24 to 48 hours, and the mode of transmission, host propensity and resistance of the virus in the environment can influence its seasonality (Kamioka et al., 2019).

In view of the importance of the Rov and Nov in the acute gastroenteritis, this study aimed to determine the occurrence of these viruses in children under five years of age presenting gastroenteritis, vaccinated or not against Rov.

2. Methodology

Children who underwent pediatric care in the service of Municipal health network of Guarapuava, Paraná State, and was prompted the investigation of the acute gastroenteritis to search for antigens Rov, parasitological or bacteriological stool culture. The inclusion of cases occurred in the municipal clinical laboratory and a total of 160 stool samples from children under five years of age were collected from March 2011 to February 2012.

The samples analyzed to determine the Rov group A was performed a reaction Multiplex Nested RT-PCR for gene VP4 using primers CON2/CON3 that amplifies 876 pb (Gentsch, 1992), for gene VP7 using the primers BEG/END that amplifies 1062 pb (Gouvea, 1990) and NoV GII was determined by RT-PCR using primers G2SKF/G2SKR specific for the N-Terminal region that amplifies 344 pb (Kojima et al, 2002).

After obtaining written parental consent, children were assessed to establish the clinical presentation and parents were asked for the child vaccination cards. The children were classified as vaccinated for rotavirus if the card had the 2 documented doses of the vaccine, and the children with one or no rotavirus vaccine dose were classified as unvaccinated.

3. Results and Discussion

In this study where evaluated the circulation of Rov and Nov in children in the community, we did not find patients infected with Rov and Nov detection rate was 11.9%. The children include had a mean of 2.8 and a median of 3 years of old and the average of Rov vaccination rate was 83.85%. Nov positives were detected mainly in September and October months of

2011 (figure 1), when an outbreak occurred in this period. Among 19 cases of Nov infection, 10 were females (52,63%) and 9 males (47,37%), as mean of 2.95 and a median 3.0 years of old.

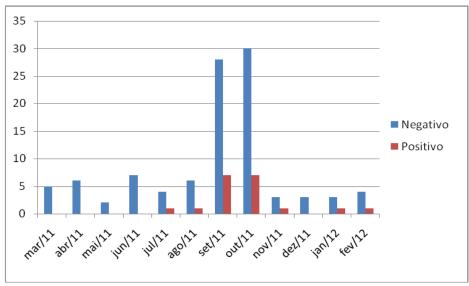


Figura 1 - Monthly distribution of the samples included in the study, according to the result in the detection for NoV.

Source: Authors (2022).

Recent studies have demonstrated the importance of Nov in humans of all ages and worldwide (Leshem et al., 2013; Ferreira et al., 2012; Cilli et al., 2011; Bucardo et al., 2011; Tuan et al., 2012). NoV in Brazil are still little studied compared to world data, the few studies investigate almost exclusively hospitalized patients and indoors (kindergartens, nursing homes), missing studies in the community, which raises questions about how these viruses are distributed in the environment (Barreto et al.; 2006). The follow-up of AGE caused by Rov plays an important role due to the need for viral circulation surveillance after vaccine implantation, as well as continuously monitoring the benefits generated by this preventive measure (Valencia et al., 2003).

According to the evaluation of Rov and Nov circulation in community children, no rotavirus-infected patients were found. Studies conducted in the hospital often report a higher incidence of rotavirus than community studies, because rotavirus infection is more severe than other etiological agents, most of the time leading the child to hospitalization (Vieira et al., 2011).

The development of effective vaccines has assumed great importance for the control of Rov infections (Patel et al., 2013). Thus, WHO recommended general vaccination in all children in the world and emphasized being essential measure in preventing this viral infection. The absence of rotavirus may be related to the vaccination rate of the children included in the study, in which it presented an overall vaccination rate of 83.8%, ranging from 56.5% to 100% according to age group. Data from the literature pointed to a general vaccination coverage in the country close to that found in this study, after the beginning of vaccination for Rov the vaccination coverage was 79.79% in 2007 to 81.18% in 2008, in 2009 it was 85.99%, 2010 it was 83.04% and 2011 with 87.12% (Domingues & Teixeira, 2013). However, it fell and reached 77% in 2020 (Nunes, 2021).

In this study the detection rate of Nov was 11.9%, in Brazil data published in the literature show varied positivity rates for Nov ranging from 8% to 39.7%. (Soares et al., 2007; Ribeiro et al., 2008; Ferreira et al., 2012; Morillo et al., 2008; Kamioka et al., 2019; Sarmento et al., 2021; Siqueira et al., 2013; Raboni et al., 2014; Amaral et al., 2015). Although this virus was first associated with AI, the lack of methods to cultivate it underestimated its importance, both in sporadic cases and in outbreaks, which could only be better detected after the development of molecular methods (Morillo et al., 2008; Morillo et al., 2011).

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4. Conclusion

In conclusion, this study demonstrated that 11,9% of the acute gastroenteritis identified in up to five years of age children was associated with NoV, while that RoV don't was identified could be related of high-rate immunization of this population.

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References

Ahmed, S. M., Hall, A. J., Robinson, A. E., Verhoef, L., Premkumar, P., Parashar, U. D., Koopmans, M., & Lopman, B. A. (2014). Global prevalence of norovirus in cases of gastroenteritis: a systematic review and meta-analysis. *The Lancet Infectious Diseases*, 14(8), 725–730.

Amaral, M. S. C. et al. (2015). The prevalence of norovirus, astrovirus and adenovirus infections among hospitalised children with acute gastroenteritis in Porto Velho, state of Rondônia, western Brazilian Amazon. *Memórias do Instituto Oswaldo Cruz*, 110, 215-221.

Atmar, R. L., Ramani, S., & Estes, M. (2018). Human noroviruses: Recent advances in a 50-year history. Current Opinion in Infectious Diseases, 31(5), 422-432

Bányai, K., Estes, M., Martella, V. & Parashar, U. (2018). Viral gastroenteritis. Lancet, 392, 175-186.

Barreto, M. L., Milroy, C. A., Strina, A., Prado, M. S., Leite, J. P., Ramos, E. A., Ribeiro, H., Alcantara-Neves, N. M., Teixeira, M. D. A. G., Rodrigues, L. C., Ruf, H.; Guerreiro, H. & Trabulsi, L. R. (2006). Community-based monitoring of diarrhea in urban Brazilian children: incidence and associated pathogens. *Tropical Medicine of Hygiene.*v.100, n.3, p. 234-242.

Bucardo, F., Lindgren, P. E., Svensson, L. & Nordgren, J. (2011). Low Prevalence of Rotavirus and High Prevalence of Norovirus in Hospital and Community Wastewater after Introduction of Rotavirus Vaccine in Nicaragua. *PLoS ONE* 6(10).

Centro De Controle E Prevenção De Doenças. (2021). Epidemiology and Prevention of vaccine- preventable diseases: *Rotavirus* (capitulo 19). https://www.cdc.gov/vaccines/pubs/pinkbook/rota.html.

Cilli, A., Luchs, A., Morillo, S. G., Costa, F. F., Carmona, R. C. & Timenetsky, M. C. S. T. (2011). Characterization of rotavirus and norovirus strains: a 6-year study (2004-2009). *Jornal de Pediatria*, 87(5), 445-449.

Clark, B. & Mckendrick, M. (2004). A review of viral gastroenteritis. Curr Opin Infect Dis 17: 461-469.

Domingues, C. M., Allan, S. & Teixeira, A. M. S. (2013). Coberturas vacinais e doenças imunopreveníveis no Brasil no período 1982-2012: avanços e desafios do Programa Nacional de Imunizações. *Epidemiologia e Serviços de Saúde*, 22(1), 9-27.

Ferreira, M. S. R., Xavier, M. D. P. T. P., Tinga, A. C. D. C., Rose, T. L., Fumiam, T. M., Fialho, A. M., Assis, R. M. D., Costa, F. A. C., Oliveira, S. A. D., Leite, J. P. G. L. & Miagostovich, M. P. (2012). Assessment of Gastroenteric Viruses Frequency in a Children's Day Care Center in Rio De Janeiro, Brazil:A Fifteen Year Study (1994–2008). *PLoS ONE*. 7(3).

Gentsch, J. R., Glass, R. I., Woods, P., Gouvea, V., Gorziglia, M., Flores, J., Das, B. K. & Bhan, M. K. (1992). Identification of group Arotavirus gene 4 types by polymerase chain reaction. *J Clin Microbiol* 30: 1365-1373.

Gouvea, V., Glass, R. I., Woods, P., Taniguchi, K., Clark, H. F., Forrester, B. & Fang Zy. (1990). Polymerase chain reaction amplification and typing of rotavirus nucleic acid from stool specimens. *Journal of Clinical Microbiology* 28: 276-282.

Kamioka, G. A. et al. (2019). Norovírus no município de São Paulo, 2010-2016: estudo transversal sobre a principal causa de gastroenterite infantil. *Epidemiologia e Serviços de Saúde*, 28, e2018290.

Kojima, S., Kageyamat, F. S., Hoshino, F. B., Shinohara, M., Uchida, K., Natori, K., Takeda, N. & Katayama K. (2002). Genogroup-specific PCR primers for detection of Norwalk-like viruses. *Journal of Virological* Methods 100: 107-114.

Leshem, E., Wikswo, M., Barclay. L., Brandt, E., Storn, W., Salehi, E., De Salvo, T., Davis, T., Sauap, A., Dobbins, G., Booth, A.H., Biggs, C., Garman, K., Woron, M.A., Parashar, D.U., Vinjé, J.& Hall, J.A. (2013). Effects and Clinical Significance of GII.4 Sydney Norovirus, United States, 2012–2013. *Emerging Infectious Diseases*. 19(8).

Lopman, B. A., Steele, D., Kirkwood, C. D. & Parashar, U. D. (2016). The Vast and Varied Global Burden of Norovirus: Prospects for Prevention and Control. *PLoS Med.* 13.

Morillo, S. G., Cilli, A., Carmona, R. D. C. & Timenetsky, M. D. O. C. (2008). Identification and molecular characterization of norovirus in São Paulo State, Brazil. Brazilian. *Journal Microbiology*. 39(4), 619-622.

Morillo, S. G., Luchs, A., Cilli, A., Ribeiro, C. D., Calux, S. J., Carmona, R. D. C. & Timenetsky, M. D. O. C. (2011). Norovirus 3rd Generation kit: an improvement for rapid diagnosis of sporadic gastroenteritis cases and valuable for outbreak detection. *Journal Virology Methods*. 173(1), 13-16.

Research, Society and Development, v. 11, n. 4, e24611427301, 2022 (CC BY 4.0) | ISSN 2525-3409 | DOI: http://dx.doi.org/10.33448/rsd-v11i4.27301

Nunes, L. (2021). Cobertura Vacinal do Brasil. Instituto de Estudos para Políticas de Saúde Panorama da Cobertura Vacinal no Brasil. https://ieps.org.br/wp-content/uploads/2021/05/Panorama_IEPS_01.pdf>.

Patel, M. et al. (2013). A systematic review of anti-rotavirus serum IgA antibody titer as a potential correlate of rotavirus vaccine efficacy. The Journal of infectious diseases, 208(2), 284-294.

Raboni, S. M. et al. (2014). Acute gastroenteritis and enteric viruses in hospitalised children in southern Brazil: aetiology, seasonality and clinical outcomes. Memórias do Instituto Oswaldo Cruz, 109, 428-435.

Ribeiro, L. R. et al. (2008). Hospitalization due to norovirus and genotypes of rotavirus in pediatric patients, state of Espírito Santo. *Memórias do Instituto Oswaldo Cruz*, 103, 201-206.

Sarmento, S. K. et al. (2021). Virological and Epidemiological Features of Norovirus Infections in Brazil, 2017–2018. Viruses, 13(9), 1724.

Siqueira, J. A. M. et al. (2013). Norovirus infection in children admitted to hospital for acute gastroenteritis in Belém, Pará, Northern Brazil. *Journal of Medical Virology*, 85(4), 737-744.

Soares, C. C. et al. (2007). Norovirus detection and genotyping for children with gastroenteritis, Brazil. Emerging infectious diseases, 13(8), 1244.

Tate, J. E. et al. (2016). Global, regional, and national estimates of rotavirus mortality in children < 5 years of age, 2000–2013. Clinical Infectious Diseases, 62(2), S96-S105.

Tuan, Z. T. C. Afsah-Hejri, L., Noor, H. M. S., Nooreliza, M. R., Naziehah, M. D., Tang, J. Y. H., Noorlis, A., Elexson, N., Chai, L. C., Ghazali, F. M., Cheah, Y. K. & Son, R. (2012). Assessment of Noroviruses in selected Ulam from local market in Malaysia. *International Food Research Journal*, 19(3), 877-882.

Valencia, R., Roman, E., Garcia-Leon, F. J. & Guillén, J. (2003). Sistemas de Alerta: Una prioridad em Vigilância Epidemiológica. *Gaceta Sanitaria*. 1(6), 20-522.

Vieira, S. C. F. et al. (2011). Acute diarrhoea in a community cohort of children who received an oral rotavirus vaccine in Northeast Brazil. *Memórias do Instituto Oswaldo Cruz*, 106, 330-334.