LETTER TO THE EDITOR

Norovirus in stool of patients with SARS-CoV-2, clinical and social importance

Norovirus en heces de pacientes con SARS-CoV-2, importancia clínica y social

Carlos E. Cabrera-Pivaral

Department of Public Health, University Center of Health Sciences, Universidad de Guadalajara; Medical Direction ME Piel Centro Dermatológico. Guadalajara, Jalisco, Mexico

To the Editor,

Diarrhea is one of the initial symptoms that can occur in SARS-CoV-2 infection (particularly with Omicron subtypes), with a mild clinical course and a duration of 1 to 3 days[1]. However, other viruses can also cause diarrhea in pediatric patients, such as norovirus, which is characterized by self-limiting diarrhea accompanied by nausea, vomiting, and abdominal pain, similar to COVID-19[2]. Considering that SARS-CoV-2 infection causes dysregulation of the immune system, this allows opportunistic infections to join the process, and noroviruses could be one of them, especially in pediatric patients. In this regard, stool samples from 123 pediatric patients aged between 2 months and 5 years with Omicron lineages BA.1, BA.2, BA.4, and BA.5, of mestizo ancestry from western Mexico, were studied. RNA was extracted from the stools to perform a real-time reverse transcriptase polymerase chain reaction (RT-PCR) test to detect noroviruses using the primers JV12Y-ATACCACTATGATGCAGAYTA and JV13I-TCATCATCACCATAGAAIGAG to amplify the norovirus RNA polymerase gene, followed by automated sequencing. Positive results were found for genotypes of the GI.1-8 group (Norwalk/68/US, Toronto 24/91/CA, VABeach/01/US) and GII.[1-17] (M7/03/US, Fayetteville/02/US) in 70.73% of cases (Table 1). The genotypic distribution was compared with that obtained from controls, which correspond to stool samples from the family members of the pediatric patients (n = 123), with RT-PCR negative for COVID-19. In controls, different genotypes of noroviruses tested positive in 16.26% (n = 20). In both cases and controls that tested positive for norovirus, no different genotypes were detected in the samples from the same person. This distribution indicates a positive association, with chi-square test = 30.3, $p < 0.0000001$, odds ratio of 1.6, confidence interval of 1.3-1.8, etiological fraction in the population of 15.9%, and etiological fraction in the exposed of 38.5%. There was intrafamilial transmission in 16.26% of cases (Table 1), with concordance in Omicron BA.2 cases of 33.3% for the Norwalk/68/US agent and 100% for the Toronto 24/91/CA genotype. In BA.4 cases, concordance with family members was 100%. In BA.5 cases, familial concordance was 100% for the Fayetteville/02/US genotype, 50% for M7/03/US, 75% for Toronto 24/91/CA, and 60% for VABeach/01/US.

The above data suggest that SARS-CoV-2 infection increases the risk of diarrhea caused by norovirus in pediatric patients. Regardless of the genotype, this is very important from both clinical and social perspectives, as diarrhea associated with gastroenteritis is one of the primary causes of medical consultation in pediatric patients. Transmission is fecal-oral, through contaminated water or food, and should be considered in the management of pediatric patients with COVID-19, as they are immunosuppressed, as well as in cases of persistent infection and also in oncological patients and immunosuppressed adults[2].

Correspondence:
Carlos E. Cabrera-Pivaral
E-mail: carlos.pivaral@academicos.udg.mx.

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Table 1. Distribution of norovirus in pediatric patients with mestizo ancestry and SARS-CoV-2 omicron infection

SARS-CoV-2 Omicron Subtype	Norovirus genotype	No. of positive subjects	Genotype concordance with family members
BA.1	Norwalk/68/US	0	0
	Toronto 24/91/CA	3	0
	VABeach/01/US	8	0
	M7/03/US	9	0
	Fayetteville/02/US	11	0
BA.2	Norwalk/68/US	6	2
	Toronto 24/91/CA	1	1
	VABeach/01/US	1	0
	M7/03/US	1	0
	Fayetteville/02/US	6	0
BA.4	Norwalk/68/US	1	0
	Toronto 24/91/CA	2	0
	VABeach/01/US	1	0
	M7/03/US	1	0
	Fayetteville/02/US	5	5
BA.5	Norwalk/68/US	13	0
	Toronto 24/91/CA	4	3
	VABeach/01/US	10	6
	M7/03/US	2	1
	Fayetteville/02/US	2	2
Family members of patients with SARS-CoV-2 Omicron	Norwalk/68/US	25	-
	Toronto 24/91/CA	6	-
	VABeach/01/US	16	-
	M7/03/US	0	-
	Fayetteville/02/US	0	-

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Conflicts of interest

None declared.

Ethical disclosures

Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained approval from the Ethics Committee for analysis and publication of routinely acquired clinical data and informed consent was not required for this retrospective observational study.

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