



## Review

## Human norovirus infection in Latin America



Tatiane da Silva Poló<sup>a,b</sup>, Juliana R. Peiró<sup>b</sup>, Luiz Cláudio Nogueira Mendes<sup>b</sup>,  
 Louisa F. Ludwig<sup>a</sup>, Edmilson F. de Oliveira-Filho<sup>a</sup>, Filemon Bucardo<sup>c</sup>, Pascale Huynen<sup>d</sup>,  
 Pierrette Melin<sup>d</sup>, Etienne Thiry<sup>a</sup>, Axel Mauroy<sup>a,\*</sup>

<sup>a</sup> *Veterinary Virology and Animal Viral Diseases, Fundamental and Applied Research on Animal and Health centre and Faculty of Veterinary Medicine, University of Liège, Belgium*

<sup>b</sup> *Department of Clinics, Surgery, and Animal Reproduction, School of Veterinary Medicine, Univ Estadual Paulista (UNESP), Araçatuba, SP, Brazil*

<sup>c</sup> *Department of Microbiology, National Autonomous University of León, Nicaragua (UNAN-León), Nicaragua*

<sup>d</sup> *Clinical Microbiology Department, University Hospital of Liège, Liège, Belgium*

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## ABSTRACT

Noroviruses are important enteric pathogens involved in non-bacterial gastroenteritis outbreaks worldwide. Noroviruses mainly occur from person to person via the fecal-oral route but also through contaminated food or water; indirect contamination is also possible due to the resistance of the virus in the environment. Latin American countries as a whole cover a vast North-to-South range, which is highly heterogeneous in terms of climate, ecosystem, human population distribution (urban areas with high human densities versus closed communities), economic development and genetic backgrounds resulting from each particular historical context. This review aims to present epidemiological and clinical patterns of human norovirus infections in Latin American countries. Divergent prevalences were observed depending on the country and the surveyed population. In particular, a shift in rotavirus/norovirus ratio in the etiologies of gastroenteritis was detected in some countries and could be attributed partly to rotavirus vaccine coverage in their infant population. While GII.4 noroviruses were seen to constitute the most common genotype, differences in genotype distribution were observed both in the environment (via sewage sampling proxy) and between genotypes circulating in healthy and diarrheic patients. Due to high climatic discrepancies, different patterns of seasonality were observed. Accordingly, this continent may condense the different particular epidemiological features encountered for HuNoV infections worldwide.

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\* Corresponding author.

E-mail address: [amauroy@ulg.ac.be](mailto:amauroy@ulg.ac.be) (A. Mauroy).

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## 1. Introduction

Infectious diarrhea, especially in children, is an important worldwide health issue, particularly in developing countries [1–3]. In most countries, human noroviruses (HuNoVs) are considered as the main viral cause of acute gastroenteritis (AGE) outbreaks in adults and as the second most common viral agent in children after group A rotaviruses (RVA) [4].

HuNoVs belong to the genus *Norovirus*, family *Caliciviridae* and are non-enveloped viruses with a positive-sense, single-stranded RNA genome. NoV strains are currently classified into seven genogroups (G), which are further subdivided into at least thirty genotypes [5–7]. Viruses belonging to GI, GII, and GIV infect humans, while GII, GIII, GIV, GV, GVI and GVII NoVs have been described in animal species [8–12]. Interestingly, few animal species share strains with human within the same genogroups (GII for porcine and GIV for canine and feline).

This review compiles data from Latin American countries and aims at the description of their particular characteristics of regarding HuNoV infections. In particular, the reviews will focus on main transmission routes, clinical aspects and (molecular) epidemiology. Each aspect will be presented from what is known from other regions of the world and confronted to the Latin American situation.

## 2. Transmission

HuNoVs are resistant in the environment and can be transmitted faecal-orally via different routes, notably by the consumption of contaminated food or water, by contact with contaminated people, objects or surfaces, or even via vomit-derived aerosols [13]. Although NoVs have been detected in animal feces, no evidence of zoonotic transmission has been reported so far [13].

River waters are at risk for HuNoV contamination as they usually receive effluents of wastewater treatment plants, which are more efficient for removal of bacteria rather than viruses [14,15]. Several studies throughout the world have detected HuNoV in river water used for irrigation as well as in drinking water [13]. While in the Amazon region, HuNoVs have been molecularly detected only at low frequencies in stream water samples from the city of Manaus, they have been shown to be responsible for AGE outbreaks following consumption of contaminated water from the river, poor hygienic behavior, or recreational activities in contaminated water [16]. In Guatemala, an AGE outbreak occurred in a student group after a school trip and its origin was traced to contaminated water consumption [17]. HuNoVs have been also detected in water from Argentinean rivers with 7.7% of positive samples from the Luján River and up to 80.8% of positive samples from the Matanza-Riachuelo River in Buenos Aires [18]. This study also showed that faecally contaminated waters frequently involve multiple genetically divergent strains. In the same country, in a study conducted on eight AGE outbreaks due to HuNoVs, three outbreaks were attributed to a waterborne origin [19], confirming that HuNoVs can constitute an issue for safe water supply. Also in Colombia, HuNoVs

have been detected in two samples from freshly treated potable water [20]. In the region of Antofagasta, Chile, AGE cases have been reported wherein HuNoVs were found both in stool samples and in environmental samples, leading to a revision of the rules concerning wastewater usage for irrigation of vegetables, especially those habitually consumed raw [21]. In Mexico, the virus was detected during spring in estuary waters [22].

The different stages of the food production (at pre-harvest, harvest and post-harvest levels) are at risk for HuNoV contamination [13]. In Rio de Janeiro, Brazil, HuNoVs were detected in six out of nine lettuce samples collected from supermarkets, food services and restaurants [23], mirroring previous observations in other countries [24–28]. In Chile, foodborne AGE outbreaks often occur following consumption of contaminated seafood products [29]. Seafood constitutes a major food supply in Latin American countries and shellfish, in particular, have been shown to concentrate HuNoVs in their digestive tissues by filtration and concentration through specific binding [30,31]. Moreover, an underestimation of the real burden of foodborne and waterborne HuNoV infections probably exists due to the frequent absence of an active surveillance system to identify and report HuNoV outbreaks in most Latin American countries [32].

Due to their low infectious dose and high environmental stability, HuNoVs are highly transmissible, rendering the person-to-person transmission route the most efficient, especially in (semi)-closed communities [13]. Sharing the same contaminated environment can obviously facilitate the transmission of this virus as exemplified by an AGE outbreaks with highly efficient person-to-person transmission reported in Peru [33], in Argentina [34] and in Brazil [35,36]. Furthermore, the person-to-person transmission route facilitates geographical extension of outbreaks caused by contaminated food as observed in Antofagasta, Chile [21], and in outbreaks involving Latin American travelers [33,37–39]. In Chile, a prevalence of 12.3% for HuNoVs in AGE outbreaks has been found, with positive detection in samples from wastewater treatment plants but negative results in potable water samples collected from households [21]. In this country, several outbreaks caused by HuNoVs have been reported from closed communities such as childcare centers, schools and hospitals, while a smaller fraction was reported to occur in restaurants [29].

## 3. Clinical aspects

After a short incubation period (1–2 days), the main symptoms reported following HuNoV infection, are vomiting, fever, diarrhea, nausea, abdominal cramps, headache, chills and myalgia [4,32,40–42], which are all usually short-term and self-limiting. Vomiting seems to be the most frequent symptom regardless of the age of patient [42,43]. Severe AGE cases, although less frequent, usually involve infants and elderly or immunocompromised patients, and can sometimes require hospitalization [32,41,44–46]. Besides the classical symptoms associated to AGE, HuNoV infections have in some cases been associated to other non-usual

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