

Cases of acute gastroenteritis due to calicivirus in outbreaks: clinical differences by age and aetiological agent

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Abstract

The *Caliciviridae* family includes norovirus and sapovirus, which both cause acute gastroenteritis (AGE). Currently, norovirus is the most common cause of AGE in all age groups in many countries. We analysed clinical differences in reported cases of acute gastroenteritis caused by caliciviruses (AGC) by age group and agent involved. We conducted a descriptive study of AGE outbreaks reported to the Public Health Agency of Catalonia (Spain) in 2010 and 2011. The odds ratios (ORs) and corresponding 95% confidence intervals (CIs) were calculated to estimate the association between clinical symptoms and age. Clinical differences between the <15 years and ≥15 years age groups were statistically significant: children more frequently presented with vomiting (OR, 3.25; 95% CI, 2.56–4.13), abdominal pain (OR, 3.27; 95% CI, 2.60–4.12), fever (OR, 1.51; 95% CI, 1.17–1.96) and nausea (OR, 1.49; 95% CI, 1.19–1.85). Comparing clinical manifestations of sapovirus and norovirus infection in children aged <15 years, cases caused by norovirus more frequently presented with vomiting and fever ($p < 0.001$), and cases caused by sapovirus more frequently presented with diarrhoea ($p = 0.013$). Determination of the clinical differences associated with cases in outbreaks according to the age of the majority of cases and the symptoms most frequently detected may aid decision making and guide aetiological investigations and the adoption of prevention and control measures.

Keywords: Children, clinical features, elderly, norovirus, outbreaks, sapovirus

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Introduction

The *Caliciviridae* family includes several RNA viruses pathogenic to humans and animals, including norovirus and sapovirus, which both cause acute gastroenteritis (AGE) in humans. Currently, norovirus is the most common cause of outbreaks of AGE in many countries [1–3] and the most common cause of sporadic gastrointestinal illnesses in adults and the second

most common cause in children [4]. Although sporadic cases of AGE due to norovirus are frequent, it also often occurs as outbreaks in various areas such as hospitals, nursing homes, kindergartens, schools, restaurants and cruise ships, among others. Norovirus transmission may be person-to-person, food-borne and fomite-borne [5]. The clinical symptoms of AGE due to norovirus are usually mild or moderate, with diarrhoea and/or vomiting that usually resolves within 24–48 h, but it may also cause severe dehydration, hospitalization and even death, especially in older people [6]. Sapovirus causes mild to moderate AGE and mainly affects young children [7,8]. Sapovirus has been detected in some foods and water [9,10], in people with gastrointestinal symptoms and in asymptomatic people. Faecal-oral transmission through contaminated foods and person-to-person transmission seem to be likely [11].

Some authors have suggested that the clinical characteristics of food-borne disease outbreaks may be useful in guiding the investigation and control of outbreaks [12]. Calicivirus infections appear to share clinical presentations and mode of transmission. Vomiting seems to be more frequent in children, and diarrhoea in adults [13]. Kaplan's clinical criteria for attributing the cause of an AGE outbreak to norovirus are vomiting in $\geq 50\%$ of cases, duration of illness 12–60 h, and a mean incubation period of 24–48 h [14]. The aim of this study was to analyse clinical differences in cases of acute gastroenteritis due to calicivirus (AGC) associated with outbreaks according to age group and agent involved in order to provide useful evidence for the detection, reporting and investigation of AGC outbreaks.

Methods

In Catalonia, a region in the northeast of Spain with 7 500 000 inhabitants, physicians must report any suspected epidemic outbreak to the Public Health Agency of Catalonia (ASPCAT). We conducted a descriptive study of AGC outbreaks reported to the ASPCAT in 2010 and 2011. An outbreak was defined as ≥ 2 cases of AGC epidemiologically linked by time and place. Only outbreaks with confirmed cases were included in the analysis. For each outbreak, we investigated the number of cases, the relationship between them and the transmission route. A confirmed case of AGC was defined as a patient with ≥ 2 loose stools and/or ≥ 2 episodes of vomiting within 24 h, with detection of sapovirus or norovirus in faeces.

Confirmed and probable cases of AGC were assessed for inclusion in the study. For each case, sociodemographic data and information about type and duration of symptoms and healthcare received were collected. Patients were asked about AGE symptoms, diarrhoea and vomiting, and additional symptoms such as nausea, fever, abdominal pain, headache, myalgia, malaise and chills. Information was collected by staff of the epidemiological research units using a standardized questionnaire. To assess clinical severity, the number of diarrhoeal stools or episodes of vomiting per day, fever, disease duration and possible hospitalization (for non-institutionalized cases only) were recorded.

Non-normal variables were defined as medians and range or interquartile range (IQR), and variables with normal distribution were defined as the mean and standard deviation. The Kruskal Wallis and Dunn tests were used to assess equality of the medians between different groups of cases according to age. The odds ratios (ORs) and corresponding 95% confidence intervals (CIs) were calculated to estimate the association

between clinical symptoms and age. The level of statistical significance was established as $\alpha = 0.05$.

Microbiological investigations were carried out by reference laboratories for food poisoning in Catalonia (Microbiology Department, Hospital Vall d'Hebron, and the laboratory of the Public Health Agency of Barcelona). For each outbreak, all stool samples were investigated if there were fewer than 10 cases, and at least 10 samples were studied in outbreaks with more than 10 cases. Faecal samples were collected during the acute phase (first 3–5 days) of infection: a minimum of 1 g of stool was collected in a sterile, plastic container without preservative. Stool samples were kept at 4°C for 2 days and frozen at -20°C until microbiological analysis, which was carried out by the reference laboratories. Samples were pre-screened using standard microbiological tests to rule out bacteria, parasites, rotaviruses and adenoviruses. Screening for norovirus was performed by qRT-PCR assays [15]. Outbreaks of possible viral aetiology that were negative for norovirus were analysed for sapovirus using quantitative real-time PCR with primers as previously described [16]. Norovirus genogroup assignment was performed after amplification by semi-nested RT-PCR of the ORF1/ORF2 junction region (region C) as previously described [17]. Sapovirus genogroup assignment was performed after nested RT-PCR amplification and sequencing [10].

Results

Of the 101 outbreaks detected, two, with 29 cases, were due to sapovirus, and 99, with 2727 cases, were due to norovirus. There were no rotavirus- or adenovirus-related outbreaks during the study period. Norovirus GII was the origin of 77.2% of outbreaks, GI of 5% and the combination of GI and GII of 4%. Sapovirus GI was the origin of the two reported outbreaks, which occurred in child care centres, with the route of transmission being person-to-person and/or fomites. The median number of samples collected for each outbreak during the study was eight (range, 1–68). Of the norovirus outbreaks, 50 were food-borne, five water-borne, and 44 person-to-person and/or fomites. The most frequent location of outbreaks of AGC was the catering environment, which was also responsible for most cases (45.6%).

Of the 2756 cases identified, 60% were female. Complete clinical information was obtained in 2365 cases (86%), who were included in the study. The cases corresponded mainly to the 15- to 64-year age group (38%), the ≥ 75 -year age group (31%) and the 65- to 74-year age group (14%). Most patients aged ≥ 75 years (73%) resided in nursing homes or social health

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