PERIODICUM BIOLOGORUM
VOL. 111, No 1, 107–112, 2009

UDC 57:61
CODEN PDBIAD
ISSN 0031-5362

Original scientific paper

# Epidemiology of Norovirus in Croatia – public health impact

**ANDREJA BARIŠIN**
**SUNČICA LJUBIN STERNAK**

Croatian National Institute of Public Health
Rockefellerova 7
10000 Zagreb, Croatia

**Correspondence:**
Andreja Barišin
Croatian National Institute of Public Health
Rockefellerova 7
10000 Zagreb, Croatia
E-mail: andrea.barisin@hzjz.hr

**Abbreviations:**
NoV- Norovirus

Received March 11, 2008.

## Abstract

***Background and Purpose:*** *Norovirus has the role of one of the main causative agents of gastroenterocolitis both in sporadic cases and epidemics. Reports of Norovirus outbreaks, individual cases and hospitalizations of the Croatian National Institute of Public Health were observed as well as school data base of the Ministry of Science, Education and Sports.*

***Results:*** *The characteristics of NoV outbreaks registered in Croatia in 2006 were presented in the aim of approximation of transmission routes and impact on health. NoV transmission by water in the particularly vulnerable school population causes serious repercussions on the health. The significance of Norovirus (NoV) in the Croatian population is indirectly proved by an 8.2% share of patients in all alimentary and hydric outbreaks.*

***Conclusion:*** *Taking into account this outcome, NoV should be reported as a separate entity, as the causative agent of communicable gastroentercolotis of nonbacterial etiology in our country.*

## INTRODUCTION

Viruses are the most common causative agents in general population *(1)*. The large Calicivirus family, which includes Norovirus, causes a significant number of alimentary and hydric outbreaks with gastrointestinal disease *(2)*. Noroviruses are found in Croatia as well as throughout the world. NoVs are classified in 5 genogroups (G I through G V), each of which contains several clusters or genotypes. People of all ages can develop G I, G II and G IV genogroups, with G II being the predominant strain in the world *(3)*. Longitudinal studies have shown that calciviruses (mostly Noroviruses), are causative agents of gastroenteritis in hospital and community-associated (outpatient, semiclosed communities) outbreaks. NoV transmission route is mostly faeco-oral. NoVs appear as extensive outbreaks, but also sporadically in medical care homes, hospitals, schools and on ships. NoV epidemics most commonly occur due to consumption of contaminated food or water. Drinking/bathing water contamination takes place in accidental mixing with sewage or technical (industrial) water *(2)*. Drinking water contamination by human faeces is the most common mechanism of transmission of pathogenic microorganisms to humans, both directly and indirectly via cooking. The main objective of testing drinking water is detecting faecal contamination and potentially pathogenic microorganisms *(3)*.

In recent years, multiple transmissions (by contaminated food, water, contact or patient's vomit) in NoV outbreaks have also been described. Despite rigorous counterepidemic and hygienic measures, NoVs have proven to be persistent and endemic among humans. Seasonality of the incidence of this extremely contagiuos virus is recognized in the term *winter vomiting disease*. Contrary to recent beliefs that this was a seasonal disease occurring mostly in cold months, studies conducted in the present decade have been pointing to NoVs as being present all year round *(4)*. During four described outbreaks of acute gastroenterocolitis in Sweden after a consumption of defrosted berries (raspberries) in 2006, infected persons were registered from January to August *(5)*.

Norovirus prevalence in the population is great, but it is still not reported routinely as a separate entity of communicable diseases in most countries. At least one half of the epidemics of acute nonbacterial gastroenterocolitis cases in the USA is caused by Noroviruses; in 2005, 298 312 people were infected, which constitutes 7.7% of the 23 million population *(6)*. In the same year Croatia registered 1745 infected persons in alimentary and hydric outbreaks (143 or 8.2% were NoV cases).

Defining gastroenteritis, regardless of the causative agent, presupposes three or more diarrheas in 24 hours; three or more vomiting episodes in 24 hours; diarrhea and at least two more symptoms or vomiting with two additional symptoms. Additional symptoms include abdominal pain and cramps, nausea, blood and mucus in stool, elevated temperature, diarrheal stool or emesis *(1)*. The clinical picture of a person with gastroenteritis caused by Noroviruses is characterized by nausea, strong profuse emesis dominating over watery diarrhea, abdominal cramps, elevated temperature or subfebrility. Incubation takes 12 to 48 hours. In children this is a medium severe or severe disease as there exists a danger of rapid dehydration, prostration or even death *(3)*.

Gastroenteritis is often brought on unexpectedly, including strong nausea and weakness. In most people it will disappear on its own, after two to three days of strong digestive symptoms. Children, in general, suffer a more extreme symptom of vomiting than adults. Emesis of »projectile« character and explosive diarrhea increase the probability of contamination of environment and transmission to other persons. Touching one such contaminated surface makes the hands carriers of Noroviruses via the mouth and into the digestive tract *(7)*.

Norovirus is an extremely infective agent, easily spread. Asymptomatic patients may transmit the infection via contaminated surfaces (desks, taps) in small semiclosed environments with many people, such as schools, homes, hospital wards, school camps, care facilities. The most vulnerable are children who easily spread the disease due to their characteristical behavior, by contaminated hands, food or water. After 12 to 48 hours (two days) of incubation, children often show symptoms of strong profuse emesis (three or more times in 24 hours), dominating over multiple watery diarrhea, abdominal cramps and elevated temperature. If the infected child is properly rehydrated, it will recover. However, the next three days the child will still be extremely contagious for the environment, while immunocompromised persons continue to extract the virus through their stool up to 14 days after the symptoms disappear *(8)*. The infected child needs to be taken out of school, hygienic conditions in school improved, any vomits cleaned up as soon as possible, and the surrounding surfaces disinfected. If necessary, the child should be hospitalized, provided therapy of its symptoms and rehydrated. The school must undertake strict measures of hygiene, hand washing and regular drinking water health safety, as well as sanitary-technical water supply measures.

Most NoV infections are transmitted by contact with infected persons outside home (56%), while only a small number by contact with members of a household with gastrointestinal symptoms (17%). Furthermore, in 47% of all patients improper health (unhygienic) habits were noted in handling food (population attributale risk fraction, PAF) *(1)*.

There is an incrasting number of epidemiological studies of drinking water and its health safety. The hydric epidemics that were so far described in the European countries point to water contamination by group GII NoV. The following transmission routes are listed: sewage outflow, passing through cracks in the ground and into, for instance, a well (individual water supply facility) for drinking water *(2)*.

At least one half of acute nonbacterial gastroenterocolitis epidemics in the USA is caused by NoVs *(6)*. According to Croatian epidemiological reports, 50% of total alimentary and hydric infections annually are salmoneloses (caused by *Salmonelle spp)*. Out of the other 50%, 64% (6 684) cases are those of gastroenterocolitis of nonbacterial etiology, which constitutes a 32% share in total alimentary and hydric infections according to the Epidemiology Service of the Croatian National Institute of Public Health (CNIPH).

Norovirus cannot be cultured, which creates problems in studying it *(9)*. In 2004 NoV detection in stool and water (commercially available enzyme immunoassay, the IDEIA Norwalk-like virus (NLV) enzyme linked immunosorbent assay (ELISA) for detecting NLV antigen in faecal samples and determining the NLV genogroup) was introduced in the Virology Department of the CNIPH. In this manner certain forms of gastroenterocolitis with unidentified causative agents can now be confirmed as etiologically known NoVs of the Caliciviridae family. Many laboratories are not equipped with NoV test, which is why the diagnosis often rests on prominent clinical symptoms and short disease duration.

## MATERIAL AND METHODS

Official reports on epidemics and individual cases of the Epidemiology Service, CNIPH, were used, as well as hospitalization reports of the Statistics Service, CNIPH.

School database (containing the number of pupils) of the Ministry of Science, Education and Sports was also utilized.

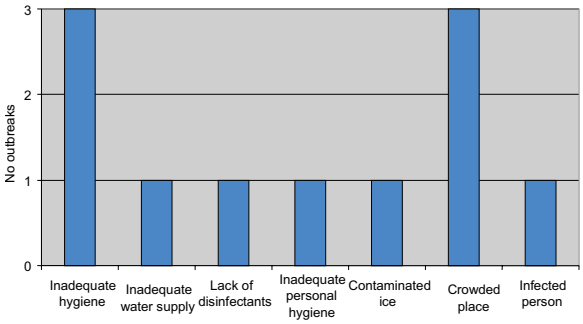


**Figure 1.** *Noro outbreaks in relation to contributing factors, 2006.*

## RESULTS

According to contributive factors, 27% of epidemics happened due to unsatisfactory hygiene and exceeding of spatial capacity (kindergarden), while lack of personal hygiene, inadequate water supply, infected person, consuming contaminated ice, lack of disinfectants and cleansing agents contributed to the development and transmission of 9% of outbreaks.

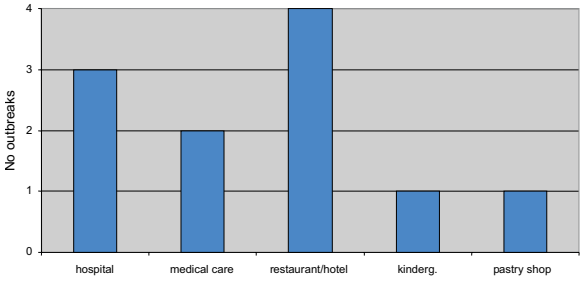


**Figure 2.** *Noro virus outbreaks by place of consumption or contamination, 2006.*

The location of outbreaks is most commonly a restaurant (in a factory, hotel; 36%), hospital ward (27%), home for aged and disabled persons (18%), and, finally, kindergarten and cake shop (9%).

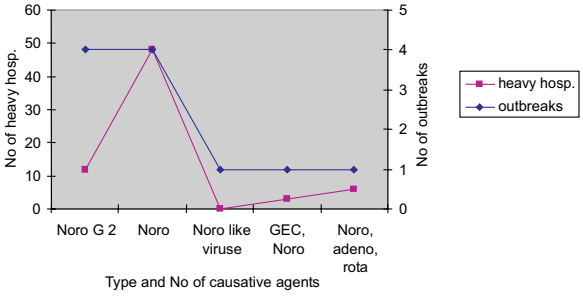


**Figure 3.** *Comparison of type and No of causative agents with heavy hospitalization.*

For the risk evaluation of NoV impact on the health status of humans a comparision of the type of NoV and the severity of clinical symptoms or the number of hospitalizations among patients could be of use. In the outbreak with three viral causative agents (Noro, Adeno, Rota) there were six severe hospitalizations (54%) out of eleven kindergarden patients, which goes to show that children are more sensitive and suffer more serious health consequences, or even death, if not provided adequate hospital therapy on time and enough hydration. In four Noro G type II *(2)* outbreaks there were 12 serious hospitalizations out of 269 registered adult patients.

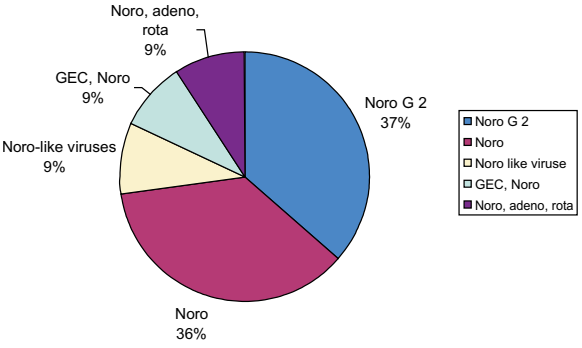


**Figure 4.** *Noro virus outbreaks by tipe and No of causative agents, 2006.*

Outbreak reports from the Epidemiology Service, CNIPH, show NoV G II *(2)* type prevalence, which coincides with the situation worldwide.

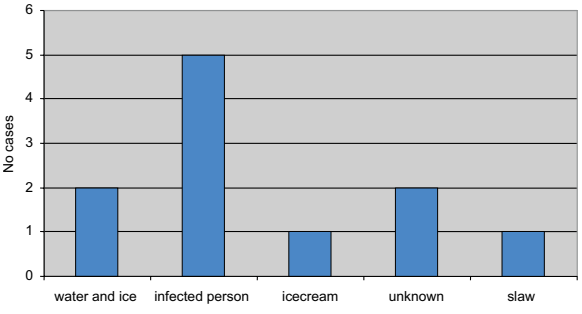


**Figure 5.** *Noro outbreaks by incriminated vehicle 2006.*

The above analyzed outbreaks show that the incriminated vehicle in 45% of cases is infected person, in 18% water and commercial ice or unknown, and 9% slaw or ice cream.

Of total hydric outbreaks by causative agent registered in the Epidemiology Service, CNIPH, 70% were cases of enterocolitis of nonbacterial viral origin in the last 7-year period, which points to the necessity of detecting types of

**TABLE 1**

Water borne outbreak.

| Year<br>Causative agent | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 |
|---|---|---|---|---|---|---|---|
| Enterocolitis | 2 | 2* | | | | 1* | 2 |
| Aeromonas aerophila | | | | | 1 | | |
| Bacillary Dysentery | | | 1 | | | | |
| Hepatitis A | | 1 | | | | | |
| Total | 2 | 3 | 1 | 0 | 1 | 1 | 2 |

* unidentified agent

causative agents. By knowing the causative agent, its characteristics and route of transmission, epidemiological studies can be used to estimate health risks and **recommend** precautionary epidemic measures.

## DISCUSSION

The main risk factor for the transmission of gastroenteritis caused by Norovirus among humans is contact with an infected person *(1)*. By analyzing NoV outbreaks in Croatia in 2006 it can be concluded that in a total of four (36.36%) outbreaks, transmission was achieved by contact with an assistant cook or due to exceeded spatial capacitites in homes and kindergardens where the epidemic spread. An important route of transmission of this resistant virus is water. Since NoV cannot be cultured, little is known today about the survival of NoV in the environment and disinfecting procedures which (safely) eliminate the virus from water and environment. NoV is moderately chlorine-resistant. Periodic laboratory testing of the safety of water in individual waterworks and wells is extremely important.

The principal goal of laboratory testing of drinking water is detection of faecal contamination. It is also possible to detect the presence of various pathogenic viruses in water, whose isolation and identification is often extremely complicated and rarely produces good results. Indirect approach is therefore assumed and virus groups or indicators evaluated to give the degree of (faecal) contamination. The most used water disinfectant is chlorine because it is available, cheap and easy to use, control and measure. After chlorine disinfection, water should be free of viruses with faecal origin, if the concentration of residual chlorine is 0.5mg/l water. This is considered minimum chlorine contact period of 30 min when acidity (pH) is below 8.0 and turbidity less than or equals 1 NTU (nephelometric turbidity unit 1-5) *(3)*. CDC recommendations: If drinking or recreational water is suspected as being an outbreak source, high-level chlorination (i.e., 10 ppm or 10 mg/L for >30 minutes) might be required for adequate disinfection; however, even this method might be insufficient in certain cases *(9)*.

English health experts estimated in January 2008 that ca. 2.8 million people were diseased by winter vomiting caused by a Norovirus, or some 200 000 people weekly, since convalescents after returning to school or work repeatedly spread the virus to other persons in their environment, thus causing hospitalization *(10)*.

The neighboring Italy, like Croatia, lacks systematic monitoring of acute nonbacterial gastroenteritis. Only until two years ago NoV was recognized as the main actor in these acute outbreaks widespread in the population, mostly among children. By analyzing the extremely high genetic mutability of NoV, we can explain the changes in epidemiological characteristics of this pathogenic microorganism in the making. According to the severity of the clinical picture, this virus can potentially even reach the level of gastroenterocolitis caused by a rotavirus in small children. What is significant is that NoV appears in 23.6% of cases in combination with one or two more viruses (rota, adeno and astrovirus), which severely worsens the clinical symptoms of the diseased *(11)*.

Among the two covered outbreaks one had three causative agents – noro, adeno and rotavirus – which resulted in serious clinical symptoms of patients and a high number of hospitalizations. According to the contributive factor, 27% of epidemics happened due to unsatisfactory hygiene and exceeding of spatial capacity (kindergarden), while lack of personal hygiene, inadequate water supply, infected person, consuming contaminated ice, lack of disinfectants and cleansing agents contributed to the development and transmission of 9% of epidemics (Figure 1).

The location of an outbreak is most commonly a restaurant (in a factory, hotel; 36%), hospital ward (27%), home for the aged and disabled persons (18%), and, finally, kindergarten and cake shop (9%) (Figure 2).

The number of persons exposed to such outbreaks, which reaches nearly 6 000 (5 885), cannot be neglected in comparison with the number of hospitalizations (473; 8%). Comparing outbreaks according to severity and number of hospitalizations with epidemics caused by one or multiple causative agents is valuable for the estimation of health risks (Figure 3). Of the total number of patients, 14.6% had severe, 30.2% medium severe and 55.4% light symptoms in their clinical picture. Persons with lighter symptoms, who recover faster, rarely see the doctor, which means that during their contagious presymptomatic and postsymptomatic period they represent a potential risk of spreading the infection in their working or school environment. In the epidemic with three mixed causative agents, 18.33% people were diseased, whereof 54.5% were hospitalized with severe symptoms of gastroenterocolitis. Outbreak reports from the Epidemiology Service, CNIPH, show NoV G II *(2)* type prevalence dominance, which coincides with the situation worldwide (Figure 4). The analyzed epidemics show that the incriminated vehicle in 45% of the cases is infected person, water and commercial ice or unknown in 18% while slaw or ice cream in 9% (Figure 5).

The magnitude of the influence of NoVs on health in winter can be worsened by an outbreak of influenza viruses circulating at that time of year among population.

Norovirus can be deadly for such vulnerable groups as children and the elderly *(10)*.

At the fourth ministerial conference on environment and health held in Budapest in 2004 the overall theme was »The Future of our Children«. CEHAPE (Children's Environment and Health Action Plan for Europe, 2004–2010) was created. The plan foresees four regional priority goals (RPGs), the first one being »to prevent and significantly reduce the morbidity and mortality arising from gastrointestinal disorders and other health effects, by ensuring that adequate measures are taken to improve access to safe and affordable water and adequate sanitation for all children.«

Croatia has 465 (19.8%) primary schools using individual water supply, which means that they receive no regular control and surveillance by the waterworks or monitoring by institutes of public health and sanitary inspection. The share of diseased Croatians in sporadically reported enteroviroses at the age 0-6 was 31.1%, and 38% at school age 7-19. Schoolchildren and younger children are specially vulnerable and their health is affected by widespread Noroviruses in population. Schoolchildren often touch contaminated joint surfaces in classrooms and toilets (desks, walls, door handles, faucets) which are not hygienic enough and represent risk factors for rapid transmission of NoVs. Most schools with individual water supply cannot afford fulltime cleaners. It is important to clean up the vomit of the infected child as the low infectious dose of NLVs (i.e., <100 viral particles *(9)*) readily allows spread by droplets, fomites, person-to-person transmission, and environmental contamination, as evidenced by the increased rate of secondary and tertiary spread among contacts and school children. NoV transmission route by contaminated droplets from the vomit to other children is large. Such unsanitary conditions in schools with individual water supply encourage future laboratory analysis of water in water supply facilities of the same schools which are not under continual public health surveillance. Alongside the above, public educational health measures (lectures and brochures) dealing with the prevention of secondary transmission of NoV causative agent are also needed. These could include extensive public actions to warn the population of:

- the importance of washing hands,
- avoiding contact with faeces,
- maximum avoidance of unnecessary touching with the person with gastrointestinal problems,
- proper hygienic procedures during cooking and food consumption,
- cleaning contact surfaces (toilets, faucets, school desks, door handles),
- staying at home during diarrheal disease (especially during an epidemic),
- regular and proper chlorination of drinking water and
- boiling water for 3 minutes before consumption in a risky area.

Sending out messages to a large public via various media (media actions: TV, radio, press, Internet) requires no great financial resources. Public health institutions already have ready mechanisms for sending out fast and successful messages about the way of controling communicable diseases to the public, which proved to be functional during various past outbreaks *(12)*. It would be useful to cooperate with county public health institutes in future research of primary schools lacking public water supply and using private waterworks (wells, local waterworks) by working together with the local community, school and family. Surveys were used to investigate the attitudes and hygienic habits of parents in relation to children with symptoms of enterocolitis. Cooperation with principals of the same schools surveys would give an insight into the sanitary-hygienic and technical situation of school water supply. The largest contribution in discovering NoV transmission by water would be obtained by laboratory analysis and detection of the presence of Noroviruses and bacteria pointing to faecal contamination and intestinal resistant parasites Crypthosporydia and G. Lambliae found in samples of water used in such schools. Of the total number of hydric outbreaks by causative agents registered at the Epidemiology Service, CNIPH, in the last 7-year period, the share of enterocolitis of nonbacterial viral origin was 70%, which points out the necessity of detecting the type of causative agent (Table 1). Only by knowing the causative agent, its characteristics and route of transmission can we more safely estimate health risks by epidemiological studies and recommend precautionary epidemic measures.

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