

Norovirus Infection

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Received on: 20/12/2021

Accepted on: 08/01/2022

How to cite this article:

Athirarani MR, Premini S/ Norovirus Infection/Indian J Comm Dis. 2022;8(1):27-31.

Abstract

Norovirus infection is a contagious virus that causes vomiting and diarrhoea. The most common symptoms of norovirus include diarrhoea, nausea, vomiting and stomach pain. Other symptoms are fever, headache and body aches. The disease is present across the world, recently cases reported from southern most part of India. The virus and multiplies in small intestine and presenting with gastrointestinal symptoms. The diagnostic measures are Real-Time RT-PCR Assay, Enzyme Immunoassays and Genotyping. Prevention and containment include mainlining the hygiene of food, fluid and practising hand hygiene.

Keywords: Norovirus; Review.

Introduction

The whole world is under the threat of COVID pandemic its first and second wave and uncertainty about the omicron variant. This resulted in people looking at every viral infection with fear and anxiety. Recent reporting of Noro Virus infection in Kerala also resulted in hue and cry among the people. Norovirus infection is also called as winter vomiting flu or stomach flu, though it has no association with influenza virus. It is very contagious virus that causes vomiting and diarrhoea. The most common symptoms of norovirus include diarrhoea, nausea vomiting and stomach pain. Other symptoms are fever, headache and body aches.¹

Epidemiology

The burden of the disease

Centre for Disease reports that worldwide, one

out of every five cases of acute gastroenteritis are caused by norovirus.² Its most common among children under the age of five years and causing an estimated number of 50,000 child deaths every year. The disease strike mostly in developing countries but it is a problem in low and high income countries. It cost \$60 billion worldwide due to healthcare costs and lost productivity.

Agent

Noroviruses were initially called as Norwalk viruses which caused an outbreak of gastroenteritis in a school in Norwalk, Ohio in 1968. Noroviruses (NoV) is a positive-sense RNA, non enveloped viruses belonging to the family Caliciviridae.³ Noroviruses has seven genogroups (GI, GII, GIII, GIV, GV, GVI, and GVII). Most noroviruses that infect humans belong to genogroups GI and GII. (31) Noroviruses from genogroup II, genotype 4 (abbreviated as GII.4) account for the majority of

adult outbreaks of gastroenteritis and often sweep across the globe.⁴

Host

People of all ages can get infected and sick with norovirus.

Environmental

There is seasonality in the norovirus infection. The incidence is higher in November to April in countries located above the equator, and from May to September in countries below the equator. The places closer to the equator, norovirus may be less seasonal.

Source of Infection and Infective Material

The virus is present in the saliva and excreta of the infected individual. Norovirus spreads through contaminated food and fluid. A very small amount of virus particle is sufficient to initiate infection.

Pathophysiology and Clinical Manifestations

Through the food and fluids virus enters the gastrointestinal tract and multiplies in small intestine. The gastrointestinal symptoms are prominent with loss of taste, nausea, forceful vomiting, watery diarrhoea, and abdominal pain. The symptoms develop between 12 and 48 hours after exposure, and it will last for 1 to 3 days. In some cases there will be weakness, muscle aches, headache, cough, or low-grade fever. Severe illness is rare. The cause of death is fluid and electrolyte imbalance especially among young children. The signs of dehydration can be decrease in urination, dry mouth and throat and feeling unusually sleepy or fussy.⁵

Diagnostic Methods

Diagnostic methods include EIA such as ELISA, reverse transcriptase PCR, and nucleic acid sequence based amplification (NASBA) tests and human faecal specimens.

Real-Time RT-PCR Assay

Diagnostic methods for norovirus focus on detecting viral RNA (genetic material) or viral antigen. Now these tests are available at all clinical and public health laboratories, and most use reverse transcription real time polymerase chain reaction (RT-qPCR) assays to detect norovirus. TaqMan-based RT-qPCR assays are the preferred method

to detect the RNA of the virus as these are very sensitive and specific and also provide estimates of viral load. This can be used to test stool, vomitus, food, water, and environmental specimens for norovirus and different oligonucleotide primer sets are used to detect genogroup I, genogroup II, genogroup VIII and GIX noroviruses.⁶ The extreme analytic sensitivity of RT-qPCR permits the detection of very low titers of virus that might be present in samples from persons without disease caused by norovirus infection ie, asymptomatic cases.⁷

Enzyme Immunoassays

Rapid commercial enzyme immunoassays (EIAs) can detect norovirus antigen in stool samples but have poor sensitivity (50 to 75%) and are not recommended for testing single samples from sporadic cases of gastroenteritis. These assays can be used for preliminary identification of norovirus when testing multiple specimens during outbreaks. However, samples that test negative should be confirmed by a second technique, such as RT-qPCR.^{8,9,10,11,12} EIA kits with high specificity (>85%) and at least moderate sensitivity (>50%) might be useful for preliminary screening of multiple faecal samples associated with an outbreak of acute gastroenteritis.¹³

Genotyping

Genetic characterization of noroviruses detected in stool and environmental samples can be very useful in epidemiologic investigations by linking cases, identifying a common source or new emerging virus strains. Norovirus can be genotyped by sequence analysis of a RT-PCR product amplified from a partial region of both the polymerase gene (region B) and capsid gene (region C) in a single reaction for either genogroup I or genogroup II viruses. All laboratories participating in CaliciNet, a national laboratory surveillance network for norovirus outbreaks is coordinated by CDC.⁶

Stool specimen

Whole stool specimens should be collected for laboratory diagnosis of norovirus and are preferred over rectal swabs because of the higher quantity of virus present in whole stool. Specimen collection for norovirus testing should begin as early as possible in an epidemiologic investigation. Ideally, whole stool specimens should be collected during the acute phase of illness ie, within 48-72 hours after onset, if this is not possible, specimens

collected later in illness or after resolution ie, up to 7-10 days after onset will also helps to diagnose and confirm norovirus infection in a suspected source case patient like food handler with a recent history of diarrhoea. Obtaining a collection of high quality diagnostic specimens is crucial for laboratory confirmation. Whole stool specimens from at least five ill persons are recommended. If specimens are taken after the acute phase of illness, the number should be increased. On the basis of test characteristics of commercially available EIAs, six specimens are required to achieve >90% sensitivity in outbreak diagnosis.^{14,15} Whole stool specimens should be kept refrigerated at 39° F (4° C) if testing occurs within 2-3 weeks and while transporting to a laboratory, it should be individually bagged and sealed and kept on ice or frozen refrigerant packs in an insulated water proof container. If testing is expected to occur more than 3 weeks after collection, then stool samples should be frozen at -4° F (-20° C) or -94° F (-70° C).¹⁶ Stool specimens should be collected as early as possible during a suspected norovirus gastroenteritis outbreak and ideally from individuals during the acute phase of illness preferably within 2-3 days of onset.¹⁷

Vomit

Specimens of vomitus can be collected to supplement the diagnostic yield from stool specimens during an investigation. Collection, storage, and transportation of vomitus specimens are the same as those for stool specimens.¹³

Serum

Serum specimens are useful during acute and convalescent phases. Serum specimens may be obtained to test for a greater than fourfold rise in IgG titre to noroviruses. Acute phase specimens should be obtained during the first 5 days after symptom onset and the convalescent phase specimens should be collected during the third to fourth week after resolution of symptoms.¹³

Environmental Specimens

RT-qPCR test enables detection of norovirus RNA in water, food, and environmental specimens however, validated methods are available only for water (at CDC) and shellfish (at FDA's Gulf Coast Seafood Laboratory). If a food or a water source is strongly suspected as the source of an outbreak, a sample should be obtained as early as possible with respect to the time of exposure and preferably stored frozen at -4° F (-20° C), and CDC or FDA should

be contacted for further guidance on testing. Water can be tested for noroviruses after concentration of large volumes (e.g., up to 100 L of water) through specially designed filters.¹⁷ Environmental surface swabs have also been demonstrated to detect norovirus RNA in specific outbreak settings.^{18,19} In case of any delay in obtaining laboratory results, use Kaplan's clinical and epidemiologic criteria to identify a norovirus gastroenteritis outbreak.²¹

Kaplan's Criteria

- Vomiting in more than half of symptomatic cases.
- Mean (or median) incubation period of 24 to 48 hours.
- Mean (or median) duration of illness of 12 to 60 hours.
- No bacterial pathogen isolated in stool culture.

Prevention and Control

There is no specific medicine to treat people with norovirus illness and only symptomatic treatment is available.¹ Hand hygiene is the single most important method to prevent norovirus infection and control its transmission. Thorough hand washing with running water and plain or antiseptic soap reduces the number of microbes on hands via mechanical removal of loosely adherent microorganisms.²⁰

Prevention and Containment of Outbreaks

Considering the highly infectious nature of norovirus, exclusion and isolation of infected persons are very important to prevent transmission of virus and limiting contamination of the environment particularly in settings where people reside in long term care facilities, acute care hospitals, cruise ships and college dormitories. The principle of isolation is to minimize contact with persons during the most infectious periods of their illness includes the acute phase of illness period following recovery usually 24-72 hours and potentially incubating persons.²² The best prevention is the containment of the infection which can be attained by practicing the following measures especially in health care setting. Some of the recommendations are:

- Isolation or cohorting precautions for outbreaks among infants and young children under 2 years should be extended even after

resolution of symptoms and for infants it can be extended up to 5 days.

- Cleaning and disinfection of frequently touched environmental surfaces and equipments like commodes, toilets, hand/bedrailing, telephones, door handles, computer equipment, and other surfaces along with cohorted areas and high-traffic clinical areas. Sodium hypochlorite solutions are widely recommended for disinfection.
- Promote hand hygiene practices among health personnel by using soap and water or ethanol based hand sanitizers especially while caring patients in the affected area.
- Surgical mask and eye protection or a full-faceshield are recommended in case of caring patients with vomiting.
- Refrain ill personnel from work for a minimum period of 48 hours after the resolution of symptoms.
- Cohorting patients during outbreaks may include placing patients in multi occupancy rooms and minimize patient movements within a ward or unit.
- Restrict symptomatic and recovering patients from leaving the patient care area and avoid social gatherings.
- Establish visitor policies for acute norovirus outbreaks and provide education to staff, patients, and visitors regarding symptoms, prevention of infection, and modes of transmission throughout outbreak.
- When a cluster of acute gastroenteritis cases is detected in the healthcare facility active case finding should be initiated and collect relevant epidemiological, clinical, and demographic data along with information on patient location and outcomes.
- If an outbreak is suspected, notification should be done to local and state health departments and include stakeholders such as clinical staff, environmental services, laboratory and healthcare facility administration, public affairs for the development of policy framework.²¹

National Outbreak Reporting System

This surveillance program monitors the reporting of foodborne, waterborne, enteric person to person, and animal contact associated disease outbreaks to CDC by state and other territorial public

health agencies. This system was previously used only for reporting food borne disease outbreaks, but now expanded to include all other enteric outbreaks, regardless of mode of transmission. Furthermore, CDC is currently implementing a national surveillance system (CaliciNet) for genetic sequences of noroviruses which may also be used to measure changes in the epidemiology of healthcare associated norovirus infections.²³

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