ejpmr, 2024, 11(8), 170-177

SJIF Impact Factor 7.065

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

NOROVIRUS: A COMPREHENSIVE REVIEW OF STRUCTURE, EPIDEMIOLOGY, SYMPTOMS, AND CONTROL MEASURES

Ali Haider[1], Saira Sattar[2]*, Saqafat Ahmad[1], Tehreem Javed[3], Muhammad Wajid[4], Naeem Akhtar[1] and Asima Ameen[5]

[1]Department of Medical Lab Technology, Faculty of Life Sciences, University of Okara, Okara 56300, Pakistan.
[2]Department of Food Science and Technology, Faculty of Life Sciences, University of Okara, Okara 56300, Pakistan.
[3]Department of Human Nutrition and Dietetics, Faculty of Life Sciences, Bahauddin Zakariya University, Multan 60800, Pakistan.
[4]Department of Zoology, Faculty of Life Sciences, University of Okara, Okara 56300, Pakistan.
[5]Department of Biochemistry, Faculty of Life Sciences, University of Okara, Okara 56300, Pakistan.

***Corresponding Author: Dr. Saira Sattar**

Department of Food Science and Technology, Faculty of Life Sciences, University of Okara, Okara 56300, Pakistan.

Article Received on 05/06/2024 **Article Revised on 25/06/2024** **Article Accepted on 15/07/2024**

ABSTRACT

Norovirus, a highly contagious virus, has significantly evolved, becoming a major global public health concern. First identified in Norwalk, Ohio, USA, in 1972, it is now the leading cause of gastroenteritis worldwide, responsible for approximately 200,000 deaths annually, predominantly in developing countries. Outbreaks are common in colder climates and confined spaces, presenting symptoms such as nausea, vomiting, and diarrhoea. The elderly are particularly vulnerable, contributing to significant healthcare and economic burdens. Recent outbreaks in the UK underscore the urgent need for effective control measures, despite challenges posed by the virus's rapid mutation rate. This literature review delves into norovirus structure, classification, epidemiology, symptoms, prevention, treatment, and laboratory diagnosis. Understanding these aspects is crucial for mitigating transmission and resurgence, particularly in healthcare settings and among susceptible populations. Effective control measures and improved diagnostic techniques are vital to combat this persistent and evolving threat to global health.

KEYWORDS: *Norovirus, Gastroenteritis, Transmission pathways, RT-PCR diagnostics, Public health measures.*

1. INTRODUCTION

This microorganism, the host-specific virus becomes progressively adept at living both inside and outside of its host environment over time by developing and adapting, placing a huge strain on our healthcare services(Bartsch et al., 2020). The virus that stands out at this time is the Norovirus (NoV). First introduced in 1972 by Dr.Albert Kapikian and colleagues at the National Institutes of Health (NIH) in the United States, it was first identified in Norwalk, Ohio, USA. For almost fifty years, the human population has been infected with this endemic virus(Bruggink et al., 2021).

Ever since it was discovered, Novovirus has been recognized as the main cause of gastroenteritis and has been linked to about two hundred thousand deaths every year, most of them in developing nations(Fang et al., 2021). Due to NoV's tendency to flourish in colder weather, outbreaks classically rise within winter. When an infection occurs, there is a short-term incubation phase of 10-51 hours before the main symptoms, which frequently start and dispersed within small groups and last for two to three days, manifest(Farahmand et al., 2022). These signs include vomiting, diarrhoea, and stomach pains.

The pathophysiology of norovirus indicates that the symptoms before reported are caused by crypt-cell hyperplasia, intestinal villi growth and blunting, and small intestine cytoplasmic vacuolization(Liao et al., 2021). With an expected 80 deaths each year, this puts the senior population (65 and over) at thoughtful risk of death. Particularly, current Norovirus epidemics in the UK have exposed that the virus is the cause of a clinical and financial burden.

Thus, controlling the dispersion of NoV epidemics and stopping its recovery is important, but in practice enormously challenging(Lucero et al., 2021). The vaccines and antivirals have proven problems because norovirus contains a high mutation rate. Following to government-advised hand cleanliness practices is an active technique(Nachamkin et al., 2021). In this literature review, we will explain the structure,

Classification, epidemiology, symptoms, prevention, treatment, and laboratory diagnosis of NoV(Sarmento et al., 2023).

2. Overview of norovirus

2.1. Classifications

Norovirus belongs to the Caliciviridae family and is also known as Norwalk-like viruses. The Caliciviridae family consist of four genera which include Norovirus, Sapovirus, Lagovirus and Vesivirus(Trainor & Bak, 2023). Both Norovirus and sapovirus exist in their particular genera, whereas other caliciviruses of veterinary consequence, such as rabbit haemorrhagic disease virus and feline calicivirus, are present in Lagovirus and Vesivirus(Winder et al., 2022).

Newly, two genera are introduced in the Caliciviridae family, which name Becovirus or Nabovirus, a bovine enteric calicivirus. These genera infect only animals while the other norovirus and Sapovirus infect both animals and humans(Lo et al., 2024).Phylogenetic study of the nucleotide sequence based on the capsid gene [VP1]. The norovirus genus is divided into five genogroups which include GI, GII, GIII, GIV and GV by using the capsid gene [VP1] which is linked with human gastroenteritis(Wu et al., 2024).

Norovirus GII consists of porcine and human strains while the GIII comprises only bovine strains, and GV contains only murine strains(Chen et al., 2024). More progress in Nov classification resulted in the appearance of a seventh genogroup (GVII) in 2015, which prolonged to 10 genogroups (GI-GX) and 49 genotypes (9 GI, 27 GII, 3 GIII, 2 GIV, 2 GV, 2 GVI and 1 genotype each for GVII, GVIII, GIX [formerly GII.15] and GX) in 2019. 60 P-types, 2 tentative P-groups, and 14 tentative P-types resulted due to partial RdRp sequencing data in addition to genogroups and genotypes(Zhang et al., 2023).

2.2. Structure

The norovirus is a single-stranded RNA genome and is small in size, non-enveloped virus. One part of its structure comprises capsid(Hanisch, 2023). The virus's outer layer, or capsid, consists of protein subunits and aids in the creation of the symmetrical icosahedron structure(Kimura-Someya et al., 2024). The capsid comprises two proteins which include VP1 and VP2 which help to cover the viral RNA of norovirus(Giancotti et al., 2022). The capsid is important for sticking to host cells, which are made up of VP1. VP2, despite its small size, is vital to the capsid's assembly.As shown in figure 1.

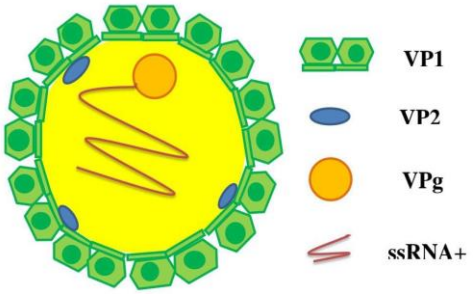

Figure 1: Norovirus structure.

The virus consists of a single-stranded positive-sense RNA genome (ssRNA+) enfold by a protein shell. The capsid is primarily made up of VP1 proteins, with minor contributions from VP2. The VPg protein is linked to the viral RNA and plays a important role in the viral replication process.

2.3. Stomach bug

The highly spreadable norovirus, also known as the "stomach bug," causes disorders in the digestive tract(Winder et al., 2022). Severe gastroenteritis caused by NoV causes severe vomiting and diarrhoea, also with nausea and cramping in the abdomen. Affected patients have dangerous stomach discomfort and trouble. It is a hazardous virus due to its rapid spread across a variation of transmission pathways, such as contaminated food, water, surfaces, and direct human contact(Carlson et al., 2024). NoV has gained a reputation as a strong and ubiquitous threat to public health as a result of its widespread. Understanding the complex dynamics of norovirus transmission exposes more than just a stomach ailment; it also reveals a powerful force that shapes public health responses and expands our knowledge of infectious diseases.

3. Epidemiology

NoV's worldwide impact is the primary cause of acute gastroenteritis, impacting millions of people each year. Increased awareness and symptom reporting are necessary due to the global impact of Nov breakouts to better epidemiological diagnosis and control efforts(Weinberg, 2019). Outbreaks caused by norovirus are frequent in severals, such as restaurants, cruise ships, medical facilities, and educational institutions.

Contaminated food, water, surfaces, and direct human contact are the main ways that the disease is spread. Because of the COVID-19 epidemic, there has been less testing and examination for other illnesses, which has resulted in a lack of reporting of endemic diseases like NoV(Lucero et al., 2021). The NoV pandemic has increased recently, according to data, and this increase has been linked to "immunity debt" and decreased exposure during lockdowns.

With a high prevalence rate and fatality risk, children under the age of five are most susceptible to NoV infection, particularly in less developed nations. Due to

patient fragility and ease of transmission among susceptible populations, healthcare facilities, notably emergency rooms and long-term care centres, are hotspots for NoV epidemics(Chen et al., 2024). In healthcare settings, close spatial layouts facilitate transmission, with symptomatic individuals identified as the primary propagation drivers. Summarise in figure 2.

During NoV epidemics, healthcare facilities bear financial strains and endanger patient safety; ward closures are a frequent result(Bonura et al., 2023). Although there isn't a vaccine to prevent NoV, research suggests that one might be developed, which would greatly lessen the financial and medical costs related to the virus. It is estimated that millions of infections may be prevented annually in the USA alone with a vaccination that is only 50% effective, underscoring the pressing need for vaccine research(Sarmento et al., 2023). Additionally, underreporting and gaps in epidemiological information of NoV are caused by the lack of routine diagnostics and surveillance in low- and middle-income countries(Wu et al., 2024). Understanding risk factors and patterns of transmission is essential, particularly in hospital settings, to reduce the effects of the NoV outbreak on at-risk populations and put effective intervention measures into place.

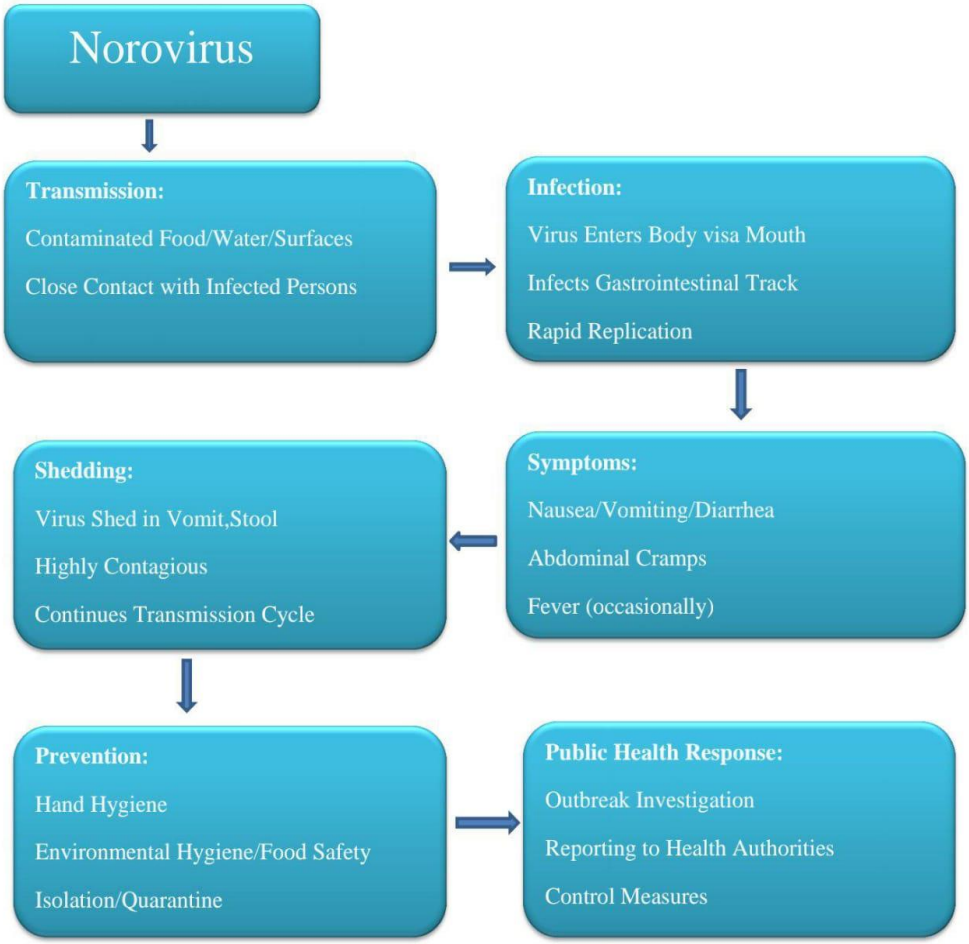

Figure 2: Norovirus Transmission and Response Cycle.

Transmission occurs thorough contaminated food, water, surfaces, and close contact with infected people. The virus enters the body orally, infects the stomach and intestines, and replicates rapidly. Symptoms include nausea, vomiting, diarrhea, abdominal cramps, and sometimes fever. Norovirus is highly contagious, with the virus shedding in vomit and stool, support the transmission cycle. Preventive measures include food safety, hand hygiene, and isolation. Public health responses focus on outbreak investigation ,notifying health authorities, and implementing control measures to prevent further spread.

4. Symptoms and complications

The gastrointestinal symptoms showthe presence NoV infection. The symptoms mostly occur within one or two days after the transmission of virus and can last for 1 to 3 days.

4.1. Symptoms

Diarrhea (frequent, watery bowel movements), Nausea (associated by uneasiness or stomach discomfort), and Vomiting (sudden, acute, often repeated episodes within a short period of time) pains or discomfort in the abdomen (ranging from minor to severe)(Ringer & Malinis, 2024). A slight fever, chills, muscle aches, and

weakness are some possible symptoms for some people. Here are a few more NoV symptoms: stomach ache or soreness, swelling and gas, decrease in appetite, losing weight, fatigue and lethargy,dizziness, headache, coughing, and sore throat runny nose, aches or stiffness in the joints, swelling of the lymph nodes, weakened muscle(Gratzl et al., 2024).

4.2. Complications

When symptoms continue for three days, they can be severe and devastating, resulting in: electrolyte differences and dehydration, malnourishment and weight loss, bacterial infections that arise later, weakening of already diagnosed illnesses, Hospitalization and mortality rates are higher in susceptible populations (elderly, young children, immune compromised individuals)(Lu et al., 2022).

4.3. Long-term symptoms

Long term symptoms include dyspepsia, irritable bowel syndrome (IBS), vomiting, spasms and abdominal pain, anxiety and depression.

4.4. When to seek medical attention

Sometimes norovirus infection can clear without using medical attention(Beredjiklian et al., 2021). But sometimes use medical attention due to severe symptoms, signs of dehydration (reduced urine output, dry mouth, dizziness), blood in stool or vomit, high fever or severe abdominal pain, alarming symptoms in vulnerable populations.

5. Transmission

5.1. Route of transmission

NoV mostly spread via the fecal-oral pathway. When an ruined person handles food with their uncovered hands, the virus can spread through the food. Food is put on a counter surface that has been infected with vomit or feces(Rushton et al., 2019). Vomit drops, the size of tiny peas, fly through the air and settle on food when someone has NoV. NoV can propagate via contaminated water as well.

This happens when an infected person vomits or defecates in the water, or when a leaking septic tank contaminates a water source, such as a well. when water is inadequately treated—for example, by using insufficient chlorine(Brown et al., 2019). When NoV-contaminated objects are left on the surface, NoV transmission can occur. Outbreaks are caused in part by direct personal contact between people, especially in crowded or enclosed environments.

5.2. Highly infectious

Norovirus is highly contagious, with a low dose necessary for infection. Even a little amount of virus can induce infection. Infected persons shed the virus in their vomit and feces(Nordgren & Svensson, 2019). This shedding begins during illness and remains for several days after recovery.

5.3. Environmental persistence

NoV can last for several days on surfaces, particularly in wet and cold environments. This virus can linger in the environment for extended periods of time, which increases the chance of outbreaks and its ability to spread(Ingle et al., 2023). Its life outside the human body is influenced by various factors, including temperature, humidity, and surface type.

5.4. Outbreaks and Settings

Epidemics can happen anywhere: in hospitals, schools, restaurants, cruise ships, etc. The crowded environments enhanced the risk of transmission. When estimating models from outbreak data, variations in symptoms (such as the early surge in infectiousness) are taken into account(Jin et al., 2020). NoV outbreaks are frequent in hospital environments because of things like immunocompromised individuals and poor cleanliness. increased hospitalization rates because of NoV gastroenteritis in patients with pre-existing chronic illnesses(Lu et al., 2020). Even while healthcare personnel probably follow greater hygiene procedures, they nevertheless play a big part in transmission.

6. Prevention

6.1. Wash your hands

Always wash your hand with soap and water for at least 20 seconds. Especially after using the restroom, changing diapers, or handling or preparing food. prior to giving medication. Even after you've recovered, it's crucial to keep washing your hands frequently(Guix et al., 2019). NoV can be detected in your poop or vomit even before symptoms show up. Still when you feel better, the virus can remain in your feces for up to two weeks, during which time you can still spread norovirus. Using hand sanitizer to treat NoV is not very effective(Guolong et al., 2021).

6.2. Handle food safely

Wash fruits and vegetables properly before preparing and eating them. Shellfish, like oysters, should be cooked all the way through to an internal temperature of at least 145°F. Keep worktops, surfaces, and cooking equipment clean and sanitized on a regular basis(Xiong et al., 2024). Note that NoV are heat-resistant, withstanding temperatures as high as 145°F. Food may not be heated enough by rapid steaming methods to eradicate NoV. Food that may have NoV contamination ought to be thrown out.

6.3. Avoid food preparation when you are sick

When you're sick, you shouldn't cook for other people or give medical attention for at least 48 hours after your symptoms go away. This also holds true for sick staff members in eateries, educational institutions, childcare centers, long-term care homes, and other establishments where they can expose patrons to NoV(Rico et al., 2020).

6.4. Disinfect surface

Even if someone throws up or has diarrhea, you should always thoroughly clean and disinfect the entire area right away. When cleaning the entire surface with paper towels, you should wear rubber gloves. After cleaning, dispose of the gloves and towel in a plastic garbage bag. After applying the bleach disinfectant to a surface for at least five to ten minutes, wash it again with hot water and soap(Mouchtouri et al., 2024). Wash your hands, take out the garbage, and fold the laundry to finish the process.

7. Laboratory diagnosis

7.1. Specimen collection

For norovirus (NoV) testing, stool specimens can be collected using Cary Blair medium or whole stools. During epidemic investigations, it is recommended to collect specimens from at least five symptomatic individuals (Korcinska et al., 2020). Stool specimens may still contain NoV even after symptoms have subsided, making it essential to follow proper collection procedures.

To gather a stool sample for analysis, begin by preparing all necessary supplies, including a paper slip, plastic container, gloves, and an alcohol cleaning pad. Ensure that each person receives a new kit (Qian et al., 2021). When collecting the specimen, if using a toilet, tape the liner in place and collect the stool. For diaper use, collect the stool with a spoon, and if the stool is liquid, use a gauze pad. Once the sample is collected, securely pack the specimen and tightly seal the container to prevent leaks.

Vomitus can also be collected during outbreak investigations, and the shipment of these specimens should be carefully arranged to ensure proper handling and preservation. Serum specimens, although generally not recommended for NoV testing, can be collected within the first five days of symptom onset (acute phase) and again during the third and fourth weeks of the convalescent phase. These serum samples should be stored at -20°C to maintain their integrity (Musin & Nikolskaya, 2021).

NoV can be detected in food, water, and environmental surfaces. For food samples, it is crucial to keep them frozen at -20°C. Water samples can be tested by passing them through filters designed for processing volumes up to 100 liters and should be stored at 4°C (Yoon et al., 2021). Hard surfaces such as kitchen counters and doorknobs can also be tested for NoV, although viruses are less abundant on these surfaces, making detection from swabs challenging. Proper specimen collection and handling are critical for accurate NoV testing and outbreak management.

7.2. Diagnostic techniques

Viral antigen or viral RNA are the diagnostic techniques used for NoV detection. All private health laboratories and many medical laboratories offer investigative tests; the most of use real-time polymerase chain reaction assays, or RT-qPCR, to identify norovirus(He et al., 2022).

7.2.1. RT-qPCR Assays

TaqMan-based on RT-qPCR assays find the virus's RNA. It can be used to check for norovirus in food, drink, feces, vomitus, and ecological specimen. Because RT-qPCR assays are so sensitive and specific, they are the method of choice for diagnosing norovirus(Nelson et al.). As low as 10–100 norovirus copies can be found by them. They identify genogroup I, genogroup II, genogroup VIII, and GIX noroviruses using distinct oligonucleotide primer sets. Viral load estimates can also be obtained using RT-qPCR tests.

7.2.2. Multiplex gastrointestinal platforms

A number of commercial technologies have recently become available for the detection of various gastrointestinal infections. They consist of the norovirus genogroups I and II. These tests' norovirus sensitivity is within the same range as that of RT-qPCR(Negrut et al., 2020).

7.2.3. Enzyme immunoassays

There are also quick and easy commercial enzyme immunoassays (EIAs) that can identify norovirus antigen in stool samples. Nevertheless, because to their low sensitivity (50 to 75%), these kits are generally not advised for analyzing individual samples from infrequent gastroenteritis cases(Zaczek-Moczydlowska et al., 2021). These tests can be utilized in multiple specimens testing during outbreaks to provide a preliminary norovirus identification. Nevertheless, samples that come out negative should be verified using a different method, like RT-qPCR. Therefore, while looking into an outbreak, EIA kits shouldn't be used in place of RT-qPCR(Chung et al., 2021).

7.2.4. Genotyping

By establishing a connection between cases, pointing to a shared source, or discovering novel virus strains, epidemiologic investigations can be conducted using the inherited categorization of noroviruses found in stool and environmental samples(Kendra et al., 2022). Sequence study of an RT-PCR product amplified from a partial area of the capsid gene (region C) and polymerase gene (region B) in a single reaction can be used to genotype noroviruses, whether they are genogroup I or genogroup II viruses. Dual typing for norovirus is used by all laboratories taking part in CaliciNet, a national laboratory observation network for norovirus outbreak run by the CDC. For typing, the acquired sequences are compared to the CaliciNet reference sequences(Cannon et al., 2021). The norovirus strain GII.4 Sydney[P16], which has been responsible for most of the norovirus outbreaks in the United States in recent years, is an illustration of dual typing nomenclature.

8. Treatment

The best course of action is to remain at home until you feel better if you suddenly start vomiting or have diarrhea. You must allow the norovirus to do its course because there is no cure. Generally speaking, you don't require medical guidance until there's a possibility of something more terrible could occur(van Kampen et al., 2022). If you or your child is experiencing symptoms, make sure you stay hydrated by drinking plenty of water. In addition to water, adults should also attempt fruit juice and soup in order to replenish the fluids lost due to vomiting and diarrhea. Electrolytes lost during vomiting and diarrhea can be replaced by consuming electrolyte-rich drinks or oral rehydration treatments. Giving children fruit juice or carbonated drinks can exacerbate their diarrhea, so avoid doing so(Tan et al., 2023). Breast milk or other types of milk feeds should be given to babies in the same manner as before. To aid in your body's healing and to bolster your immune system, get lots of sleep. In addition, paracetamol can be used to treat fever and aches and pains(Yao et al., 2020). Obtain sufficient sleep if you have symptoms of drying out, such as a dry mouth or dark urine, use specialized rehydration drinks that are sold at community pharmacies(Ahmed et al., 2020). Try simple things like bread, rice, spaghetti, and soup if you're in the mood to eat. Infants and small children—particularly those under a year old—have a higher.

If you believe you or your child has norovirus, you usually don't need to see your doctor because there isn't a specific treatment for it. Since norovirus is caused by a virus, antibiotics will not be helpful(Ingle et al., 2023).

9. CONCLUSION

In conclusion, norovirus remains a formidable public health challenge, causing significant morbidity and mortality due to acute gastroenteritis worldwide. The virus's ability to thrive in colder climates and its high mutation rate complicates prevention and treatment efforts. Effective hand hygiene, safe food handling practices, and rapid identification of outbreaks are critical to controlling its spread. Despite ongoing research, the lack of a vaccine and effective antiviral treatments underscores the need for continued vigilance and innovation in public health strategies. Understanding the complex dynamics of norovirus transmission and its impact on healthcare systems is essential for developing robust interventions to reduce the global burden of this pervasive pathogen.

Future research should focus on developing more effective vaccines and antiviral treatments to combat norovirus. Given the virus's rapid mutation rate, continuous monitoring and genetic analysis are essential to stay ahead of emerging strains. Additionally, improving diagnostic techniques will enable quicker and more accurate detection, facilitating timely intervention and reducing transmission. Public health strategies must also emphasize education on hygiene practices and the importance of vaccination, particularly in vulnerable populations and healthcare settings. By addressing these areas, we can significantly reduce the impact of norovirus and enhance global health resilience against this persistent and evolving threat.

10. REFERENCES

1. Ahmed, H., Maunula, L., & Korhonen, J. Reduction of norovirus in foods by nonthermal treatments: A review. *Journal of food protection*, *2020; 83*(12): 2053-2073.
2. Bartsch, S. M., O'Shea, K. J., & Lee, B. Y. The clinical and economic burden of norovirus gastroenteritis in the United States. *The Journal of infectious diseases*, 2020; *222*(11): 1910-1919.
3. Beredjiklian, C., Olf, M., Abusaman, A., Becker, R., & Jonescheit, J. Case report: Colon ischemia and perforation as a result of Norovirus infection. *International Journal of Surgery Case Reports*, 2021; *78*: 85-87.
4. Bonura, F., Filizzolo, C., Pizzo, M., Sanfilippo, G. L., Cacioppo, F., Palazzotto, E., Di Bernardo, F., Collura, A., Martella, V., & De Grazia, S. Biological Specimen Banking as a Time Capsule to Explore the Temporal Dynamics of Norovirus Epidemiology. *Viruses*, *2023; 15*(12): 2303.
5. Brown, J. R., Roy, S., Shah, D., Williams, C. A., Williams, R., Dunn, H., Hartley, J., Harris, K., & Breuer, J. Norovirus transmission dynamics in a pediatric hospital using full genome sequences. *Clinical Infectious Diseases*, *2019; 68*(2): 222-228.
6. Bruggink, L. D., Garcia-Clapes, A., Tran, T., Druce, J. D., & Thorley, B. R. (2021). Decreased incidence of enterovirus and norovirus infections during the COVID-19 pandemic, Victoria, Australia, 2020.
7. Cannon, J. L., Bonifacio, J., Bucardo, F., Buesa, J., Bruggink, L., Chan, M. C.-W., Fumian, T. M., Giri, S., Gonzalez, M. D., & Hewitt, J. Global trends in norovirus genotype distribution among children with acute gastroenteritis. *Emerging Infectious Diseases*, *2021; 27*(5): 1438.
8. Carlson, K. B., Dilley, A., O'Grady, T., Johnson, J. A., Lopman, B., & Viscidi, E. A narrative review of norovirus epidemiology, biology, and challenges to vaccine development. *npj Vaccines*, *2024; 9*(1): 94.
9. Chen, D., Shao, Q., Ru, X., Chen, S., Cheng, D., & Ye, Q. Epidemiological and genetic characteristics of norovirus in Hangzhou, China, in the postepidemic era. *Journal of Clinical Virology*, *2024; 172*: 105679.
10. Chung, S., Breshears, L. E., Gonzales, A., Jennings, C. M., Morrison, C. M., Betancourt, W. Q., Reynolds, K. A., & Yoon, J.-Y. Norovirus detection in water samples at the level of single virus copies per microliter using a smartphone-based fluorescence microscope. *Nature Protocols*, *2021; 16*(3): 1452-1475.
11. Fang, Y., Dong, Z., Liu, Y., Wang, W., Hou, M., Wu, J., Wang, L., & Zhao, Y. Molecular epidemiology and genetic diversity of norovirus among

hospitalized children with acute gastroenteritis in Tianjin, China, 2018–2020. *BMC Infectious Diseases*, *2021; 21*: 1-9.
12. Farahmand, M., Moghoofei, M., Dorost, A., Shoja, Z., Ghorbani, S., Kiani, S. J., Khales, P., Esteghamati, A., Sayyahfar, S., & Jafarzadeh, M. Global prevalence and genotype distribution of norovirus infection in children with gastroenteritis: a meta-analysis on 6 years of research from 2015 to 2020. *Reviews in medical virology*, *2022; 32*(1): e2237.
13. Giancotti, G., Nannetti, G., Padalino, G., Landini, M., Santos-Ferreira, N., Van Dycke, J., Naccarato, V., Patel, U., Silvestri, R., & Neyts, J. Structural investigations on novel non-nucleoside inhibitors of human norovirus polymerase. *Viruses*, *2022; 15*(1): 74.
14. Gratzl, S., Cartwright, B. M. G., Rodriguez, P. J., Do, D., Baker, C., & Stucky, N. (2024). Monitoring Report: Viral Gastroenteritis-April 2024 Data. *medRxiv*, 2024.2005. 2021.24307632.
15. Guix, S., Pintó, R. M., & Bosch, A. Final consumer options to control and prevent foodborne norovirus infections. *Viruses*, *2019; 11*(4): 333.
16. Guolong, Y., Tianmu, C., Yuanzhao, Z., Rongjie, S., Fengren, L., Bili, Y., Feng, L., & Haiduan, L. Effect of prevention and control measures of a norovirus infectious outbreak based on dynamic model. *Disease Surveillance*, 2021; *36*(12): 1312-1318.
17. Hanisch, F. G. Revised structure model of norovirus-binding fucoidan from Undaria pinnatifida: oligofucose chains branch off from a β6-galactane. *Glycobiology*, 2023; *33*(7): 556-566. https://doi.org/10.1093/glycob/cwad039
18. He, T., Chen, X., Deng, Y., Li, B., Wang, H., Wang, Q., Zhai, A., Shi, L., Chen, Y., & Wu, C. Development and validation of an efficient nomogram for risk assessment of norovirus infection in pediatric patients. *European Journal of Clinical Microbiology & Infectious Diseases*, *2022; 41*(12): 1433-1443.
19. Ingle, H., Makimaa, H., Aggarwal, S., Deng, H., Foster, L., Li, Y., Kennedy, E. A., Peterson, S. T., Wilen, C. B., & Lee, S. IFN-λ derived from nonsusceptible enterocytes acts on tuft cells to limit persistent norovirus. *Science Advances*, *2023; 9*(37): eadi2562.
20. Jin, M., Wu, S., Kong, X., Xie, H., Fu, J., He, Y., Feng, W., Liu, N., Li, J., & Rainey, J. J. Norovirus outbreak surveillance, China, 2016–2018. *Emerging Infectious Diseases*, *2020; 26*(3): 437.
21. Kendra, J. A., Tohma, K., & Parra, G. I. Global and regional circulation trends of norovirus genotypes and recombinants, 1995–2019: A comprehensive review of sequences from public databases. *Reviews in medical virology*, *2020; 32*(5): e2354.
22. Kimura-Someya, T., Katsura, K., Kato-Murayama, M., Hosaka, T., Uchikubo-Kamo, T., Ihara, K., Hanada, K., Sato, S., Murayama, K., & Kataoka, M. Structural analyses of the GI. 4 norovirus by cryo-electron microscopy and X-ray crystallography revealing binding sites for human monoclonal antibodies. *Journal of Virology*, *2024; 98*(5): e00197-00124.
23. Korcinska, M., Bjerre, K. D., Rasmussen, L. D., Jensen, E. T., Fischer, T. K., Barrasa, A., & Ethelberg, S. Detection of norovirus infections in Denmark, 2011–2018. *Epidemiology & Infection*, *2020; 148*: e52.
24. Liao, Y., Hong, X., Wu, A., Jiang, Y., Liang, Y., Gao, J., Xue, L., & Kou, X. Global prevalence of norovirus in cases of acute gastroenteritis from 1997 to 2021: an updated systematic review and meta-analysis. *Microbial Pathogenesis*, *2021; 161*: 105259.
25. Lo, M., Doan, Y. H., Mitra, S., Saha, R., Miyoshi, S.-i., Kitahara, K., Dutta, S., Oka, T., & Chawla-Sarkar, M. Comprehensive full genome analysis of norovirus strains from eastern India, 2017–2021. *Gut Pathogens*, 2024; *16*(1): 3.
26. Lu, M.-C., Lin, S.-C., Hsu, Y.-H., & Chen, S.-Y. Epidemiology, clinical features, and unusual complications of norovirus infection in Taiwan: what we know after rotavirus vaccines. *Pathogens*, *2022; 11*(4): 451.
27. Lu, Y., Ma, M., Wang, H., Wang, D., Chen, C., Jing, Q., Geng, J., Li, T., Zhang, Z., & Yang, Z. An outbreak of norovirus-related acute gastroenteritis associated with delivery food in Guangzhou, southern China. *BMC Public Health*, *2020; 20*: 1-7.
28. Lucero, Y., Matson, D. O., Ashkenazi, S., George, S., & O'Ryan, M. Norovirus: facts and reflections from past, present, and future. *Viruses*, *2021; 13*(12): 2399.
29. Mouchtouri, V. A., Simou, E., Soteriades, S., Rousou, X., Kontouli, K. M., Kafetsouli, D., Kourentis, L., Anagnostopoulos, L., & Hadjichristodoulou, C. Systematic literature review and meta-analysis on preventing and controlling norovirus outbreaks on cruise ships, 1990 to 2020: calling for behaviour change strategies of travellers. *Eurosurveillance*, *2024; 29*(10): 2300345.
30. Musin, M., & Nikolskaya, M. Norovirus infection: clinic and diagnosis in modern conditions. *Scientific Bulletin of the Omsk State Medical University*, *2021; 1*(4): 126-133.
31. Nachamkin, I., Richard-Greenblatt, M., Yu, M., & Bui, H. Reduction in sporadic norovirus infections following the start of the COVID-19 pandemic, 2019–2020, Philadelphia. *Infectious diseases and therapy*, *2021; 10*: 1793-1798.
32. Negrut, N., Khan, S. A., Bungau, S., Zaha, D. C., Anca, C. A., Bratu, O., Diaconu, C. C., & Ionita-Radu, F. Diagnostic challenges in gastrointestinal infections. *Rom J Mil Med*, *2020; 123*: 83-90.
33. Nelson, A., Bradley, L. N., Rybka, T. P., Alexander, L., Wilfert, R. A., & MacDonald, P. D. Laboratory Diagnosis: An Overview.

34. Nordgren, J., & Svensson, L. Genetic susceptibility to human norovirus infection: an update. *Viruses*, *2019; 11*(3): 226.
35. Qian, X. F., Duan, A. L., Huang, R. X., Li, N. X., Li, Y. P., & Guo, X. G. Pooled analysis of LAMP assay for the diagnosis of norovirus infection. *Journal of Clinical Laboratory Analysis*, *2021; 35*(9): e23919.
36. Rico, E., Pérez, C., Belver, A., Sabaté, S., Razquin, E., De Benito, J., Coronas, L., Domínguez, A., Jané, M., & Alsedà, M. Norovirus detection in environmental samples in norovirus outbreaks in closed and semi-closed settings. *Journal of Hospital Infection*, *2020; 105*(1): 3-9.
37. Ringer, M., & Malinis, M. Norovirus Infection in Transplant Recipients. *Current Infectious Disease Reports*, 2024; 1-6.
38. Rushton, S. P., Sanderson, R. A., Reid, W. D., Shirley, M. D., Harris, J. P., Hunter, P. R., & O'Brien, S. J. Transmission routes of rare seasonal diseases: the case of norovirus infections. *Philosophical Transactions of the Royal Society B*, *2019; 374*(1776): 20180267.
39. Sarmento, S. K., de Andrade, J. d. S. R., Malta, F. C., Fialho, A. M., Mello, M. d. S., Burlandy, F. M., & Fumian, T. M. Norovirus Epidemiology and Genotype Circulation during the COVID-19 Pandemic in Brazil, 2019–2022. *Pathogens*, *2023; 13*(1): 3.
40. Tan, M. T. H., Gong, Z., & Li, D. Use of zebrafish embryos to reproduce human norovirus and to evaluate human norovirus infectivity decay after UV treatment. *Applied and Environmental Microbiology*, *2023; 89*(4): e00115-00123.
41. Trainor, E., & Bak, A. UK guidelines for the management of norovirus outbreaks in acute and community health and social care settings 2023. *Journal of Hospital Infection*, *2023; 136*: 125-126.
42. van Kampen, J. J., Dalm, V. A., Fraaij, P. L., Oude Munnink, B. B., Schapendonk, C. M., Izquierdo-Lara, R. W., Villabruna, N., Ettayebi, K., Estes, M. K., & Koopmans, M. P. Clinical and in vitro evidence favoring immunoglobulin treatment of a chronic norovirus infection in a patient with common variable immunodeficiency. *The Journal of infectious diseases*, *2022; 226*(10): 1781-1789.
43. Weinberg, G. A. Outbreak epidemiology: one of many new frontiers of norovirus biology. In: Oxford University Press US, 2019; 219: 1349-1352
44. Winder, N., Gohar, S., & Muthana, M. Norovirus: an overview of virology and preventative measures. *Viruses*, *2022; 14*(12): 2811.
45. Wu, C., Fu, Z., Xie, C., Zhao, J., He, F., Jiao, B., & Jiao, B. Epidemiological Characteristics and Genotypic Features of Rotavirus and Norovirus in Jining City, 2021–2022. *Viruses*, *2024; 16*(6): 925.
46. Xiong, H., Ma, F., Tang, D., & Liu, D. Measures for preventing norovirus outbreaks on campus in economically underdeveloped areas and countries: evidence from rural areas in Western China. *Frontiers in Public Health*, *2024; 12*: 1406133.
47. Yao, B., Luo, Z., Xiong, W., Song, B., Zeng, Z., & Zhou, Y. Disinfection techniques of human norovirus in municipal wastewater: Challenges and future perspectives. *Current Opinion in Environmental Science & Health*, 2020; *17*: 29-34.
48. Yoon, S. H., Kim, H. R., & Ahn, J. G. Diagnostic accuracy of immunochromatographic tests for the detection of norovirus in stool specimens: A systematic review and meta-analysis. *Microbiology Spectrum*, 2021; *9*(1), 10.1128/spectrum. 00467-00421.
49. Zaczek-Moczydlowska, M. A., Beizaei, A., Dillon, M., & Campbell, K. Current state-of-the-art diagnostics for Norovirus detection: Model approaches for point-of-care analysis. *Trends in Food Science & Technology*, *2021; 114*: 684-695.
50. Zhang, P., Xu, D., Liu, T., Chen, L., & Ji, L. (2023). Genetic characterization of rarely reported GII. 3 [P25] norovirus strain detected in patients with acute gastroenteritis in Huzhou, China, *Virologica Sinica*, 2021; *38*(4): 646.