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A Study on Norovirus-Related Research

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Abstract

Norovirus is a major cause of viral diarrhea by foodborne infection. Its rapid mutation is mainly based on gene mutation, recombination. We will analyze from 4 aspects, structure and evolutionary characteristics, epidemic, main detection methods, current preventions. According to the study, pre-school children are vulnerable to norovirus each year in the child-care institutions. And the main detection is through fluorescent RT-PCR, and there are no approved vaccines or specific therapeutics to treat the disease.

Keywords: Norovirus, disease burden, detection methods

1. Introduction

Norovirus was initially discovered in fecal samples from gastroenteritis patients during an outbreak in Norwalk, hence its early designation as the Norwalk virus. It belongs to a group of morphologically similar antigenic particles with slight variations in antigenicity (Robilotti, Elizabeth, Deresinski, Stan, Pinsky & Benjamin A., 2015). Norovirus was first discovered in 1968 and has since spread globally, exhibiting distinct seasonal patterns with a higher incidence during cold seasons. The primary affected populations are adults and school-age children. The main symptoms after infection include vomiting and diarrhea. The symptoms of the infection are self-limiting (Zhao Ji, 2018). China reported its first case of a norovirus infection-related gastroenteritis outbreak in 1995 (Na Wei, Jun Ge & Changyao Tan, 2021). Subsequently, multiple norovirus infections occurred throughout the country, and it has been annually prevalent in a seasonal pattern since then. (He Fei & Shen Yongming, 2022)

2. Structure and Evolutionary Characteristics

Norovirus belongs to the Caliciviridae family, with a diameter of approximately 26-35 nm. It is non-enveloped, appearing as spherical, foam-like particles under an electron microscope. The surface exhibits a concave-convex arc-like structure. The genome is a positive-sense single-stranded RNA virus with a total length of about 7.7 kb, containing three open reading frames (ORF1, ORF2, and ORF3). ORF1 primarily encodes non-structural proteins essential for virus replication and translation, including RNA polymerase. ORF2 predominantly encodes the structural protein VP1, constituting the capsid protein, while ORF3 primarily encodes the structural protein VP2 (Liao Yingyin, Xue Liang & Gao Junshan, 2021).

The viral capsid displays an icosahedral structure, consisting of 180 VP1 proteins and 1-2 VP2 proteins. VP1 proteins can autonomously assemble, forming virus-like particles utilized as antigens for detecting specific antibodies in serum. (Natalie Winder, Sara Gohar & Munitta Muthan, 2022)

Norovirus is categorized into five genotypes determined by the diversity of VP1, specifically GI to GV. Throughout the evolutionary process, each genotype further branches into several subtypes. Precisely, GI comprises 14 subtypes, GII encompasses 17 subtypes, GIII has 2 subtypes, and both GIV and GV have 1 subtype each (Yao Xin & Liang Zhenglun, 2018). Among these, GI, GII, and GIV are known to infect humans, while GIII and GV primarily infect cattle and mice (Preeti Chhabra, Miranda de Graaf & Gabriel I. Parra, 2019), respectively. Norovirus undergoes rapid mutation and variation during its prevalence through genetic mutations and recombination. The process of genetic recombination plays a significant role in generating more genotypes during the virus's evolution. (Zheng Yan & Cui Lihong, 2016)

3. Epidemiology of the Virus

Norovirus circulates annually in human populations and is one of the main pathogens causing outbreaks of human infectious gastroenteritis and acute diarrhea in infants and young children, resulting in a certain disease burden. Norovirus can be sourced from symptomatic and asymptomatic individuals, as well as healthy carriers. The virus primarily spreads through contaminated water and food that have come into contact with feces. The primary transmission route is fecal-oral, and the population is generally susceptible. Among the three genotypes of norovirus that infect humans, the GI and GII genotypes are linked to foodborne infections. Specifically, the GII genotype is the predominant strain and is more prone to causing person-to-person infections (Zhang Chao, Deng Jianjun & Zhang Ruijuan, 2017). Norovirus exhibits seasonal patterns, with a higher incidence during the winter season. Low temperatures are favorable for norovirus infection. Following infection, there is a latent period of 12 to 48 hours. The disease is characterized by a rapid onset and a short course. Clinical symptoms in patients show a clear relationship with the health status of the infected individuals, manifesting as asymptomatic or with noticeable gastrointestinal symptoms. Norovirus infection mechanisms are relatively clear. The virus primarily invades the upper section of the jejunum without causing alterations to the patient's gastric fundus and gastric antrum. Observable changes in the structure and function of small intestinal villi result in an elevation of osmotic pressure within the intestinal cavity. This, in turn, leads to fluid entering the intestines, causing diarrhea and temporary carbohydrate malabsorption. In severe cases, it may result in electrolyte imbalance in patients. These symptoms typically exhibit a self-limiting nature, and the lesions generally fully recover in approximately 1 to 2 weeks. (Hong Xiaojing, Xue Liang & Huang Dandan, 2022)

Each year, among all cases of non-bacterial gastroenteritis, outbreaks in the United States are attributed to norovirus, accounting for as much as 60-90% of the incidents. Similar trends are observed in developed countries such as the Netherlands, the United Kingdom, Japan, Australia, and others. In China, norovirus infections are relatively common. Surveys of serum antibody levels in the population indicate a widespread prevalence of norovirus infections. Additionally, among children under 5 years old, the detection rate of norovirus is around 15%. The prevalence of norovirus infection is correlated with hygiene conditions. In situations with better hygiene conditions, the prevalence of norovirus infection tends to improve. (Honglu Zhou, Songmei Wang & Lorenz von Seidlein, 2019)

Norovirus is prevalent in China with no significant regional differences. A review of recent literature reveals that norovirus has a substantial prevalence in childcare institutions, imposing a considerable disease burden on infants and young children. Research conducted in the Fuzhou region from 2016 to 2021 indicates that norovirus primarily infects children under the age of 5, with the GII-type norovirus being the predominant circulating strain (Wu Bingshan, Huang Zhimiao & Lin Weidong, 2023). Similarly, from 2012 to 2020, there were 37 outbreaks of norovirus in Lin'an, Hangzhou, with GII genotypes also being the predominant circulating strains in 34 of the outbreaks, while the remaining 3 were caused by GI genotypes. The overall incidence rate among patients was 3.76%, and the distribution pattern showed the highest incidence rate in childcare institutions (Shi Shuilang, Lv Lei & Duan Tianxiao, 2022).

Research on norovirus outbreaks in Wanzhou, Chongqing, from 2015 to 2021 revealed a total of 14 incidents, primarily caused by GII genotypes in 13 of them, with the remaining one attributed to GI infection (Lang Zhongkai, Gan Yulu & Yan Zhaoyang, 2022). The main affected population was also in childcare institutions (Lang Zhongkai, Tan Wenli & Gan Yulu, 2023). In the years 2019-2020, a total of 2358 cases of norovirus infection were detected in Ningxia. Research indicates a detection rate of approximately 13.44%, with the predominant circulating strain being of the GII genotype (Wei Kaixin, Shi Anqi & Cao Yan, 2023). From 2016 to 2020, a total of 3120 cases of norovirus infection were detected in Changzhou City. The detection rate of norovirus was highest among preschool children in the infected population (Fan Ping, Wang Ermei & Chen Baolin, 2023). From 2017 to 2020, there were a total of 168 incidents of norovirus infection in Changping, Beijing, with a cumulative total of 1876 cases (Jin Wenjun, Wang Ruiqin & Cai Xu, 2022). From 2017 to 2021, in Beijing's Fengtai District, there were a total of 612 cases of norovirus infection, with an infection rate of 19.6%. The proportion of detected genotypes of the infecting norovirus was 14.9% for the GII genotype and 4.7% for the GI genotype, with the GII genotype being predominant (Zhao Jingjing, Wang Jiajia & Xiao Guiyong, 2023). In summary, norovirus infection is prevalent in the human population, with the GII genotype as the predominant circulating strain. Outbreaks are more likely to occur in childcare institutions, leading to a higher incidence among children.

4. Virus Detection Methods

The diagnosis of norovirus typically relies on positive laboratory test results. The commonly tested specimens include the patient's vomit and feces, as well as anal swabs. The collected specimens can be stored short-term at 4°C, while for long-term storage, they should be kept at -20°C to -70°C. Currently, serum samples from patients are not routinely used for diagnosis. The methods employed for norovirus detection include electron microscopy, immunological techniques, and molecular biology methods. Each of these methods has its limitations, although they all offer effective means for norovirus detection. Norovirus is easily detectable but challenging to culture. Currently, there is no widely recognized effective method for cultivating a large quantity of norovirus, and the selection of cells suitable for norovirus cultivation is also limited.

Electron microscopy was initially employed for norovirus detection. However, due to its intricate procedures and susceptibility to virus concentration variations in specimens, it is no longer the primary method for diagnosing norovirus infections. Common immunological methods for norovirus detection include the Elisa method and immunochromatographic techniques. Both methods rely on the specific binding characteristics of antigen-antibody interactions for detection. These methods are relatively simple to operate, with the detection specificity of the reagent kits designed for these methods being 90.6%-96.4% and 87.5%, and sensitivities being 43.8%-97.1% and 83.3%, respectively. Both methods can provide reasonably accurate detection results, but false positives and false negatives may occur due to antigenic variation in the virus during evolution, making them challenging to avoid. Molecular biology methods are currently the commonly used techniques for norovirus detection and are often referred to as the "gold standard" for virus diagnosis. These include conventional RT-PCR, multiplex RT-PCR, and fluorescence RT-PCR methods. Fluorescence RT-PCR is currently more widely used due to its high sensitivity, simplicity in operation, short result acquisition time, and convenient result interpretation. Various reagent kits are available on the market for selection. However, the specificity and sensitivity of this method depend on the primers and probes used. Therefore, it is essential to timely update with better-matched primers and probes based on the virus's variation. (Sun Zhiqiang, Huang Zhicheng & Wang Xiu, 2020)

5. Disease Prevention and Control Status

The general population is generally susceptible to norovirus infection, and common symptoms following infection include digestive system symptoms such as diarrhea, vomiting, and nausea. It can also lead to systemic symptoms such as fever, headache, chills, and muscle pain. Severe diarrhea can result in fluid imbalance, electrolyte disturbances, and symptoms of dehydration in the human body. Typically, after infection, children commonly exhibit symptoms such as vomiting and nausea, while adults primarily experience diarrhea, often in the form of watery or loose stools. Vomiting is less common in adults. The disease course usually lasts 2-3 days, and it is a self-limiting illness with

a good prognosis. After norovirus infection, some patients can recover without the need for medication. Currently, there are no specific antiviral drugs for the treatment of norovirus infection in clinical practice. Treatment primarily focuses on symptomatic relief. Patients with severe symptoms should seek medical attention promptly, and treatment may involve fluid replacement therapy. Due to the rapid variability of norovirus, the antibodies produced after infection lack long-term protective effects. Currently, there is no developed vaccine for preventing norovirus infection effectively (Ford-Siltz, Lauren A. Tohma, KentaroParra & Gabriel I, 2021). As a result, the population may experience repeated infections with the annually circulating norovirus. It is advisable to pay attention to hand hygiene, food safety, strengthen preventive awareness, and thereby effectively avoid viral infections.

6. Conclusion

Norovirus is one of the main causative agents of foodborne illnesses, and infections are relatively common. The virus exhibits strong variability during its prevalence and is prone to causing cluster infections. In daily life, we should enhance hygiene awareness, making efforts to avoid viral infections as much as possible. The structural and genetic attributes of the virus have undergone comprehensive examination. Utilizing the evolutionary traits of the VP1 gene, genotypes have been meticulously categorized. Recent detection outcomes indicate the prevailing presence of the GII genotype in the prevalence of norovirus. Presently, the detection technology for norovirus has reached a level of maturity. The fluorescence reverse transcription-polymerase chain reaction (RT-PCR) method stands out as a widely employed, operationally convenient, and highly accurate diagnostic technique. The timely testing of excreta from infected patients is imperative for disease diagnosis and holds considerable significance in guiding clinical treatment. Although gastrointestinal symptoms such as vomiting and diarrhea are typical manifestations of norovirus infection, it is crucial to recognize the potential for severe cases that may pose a life-threatening risk. Considering the broad susceptibility of the population, it is imperative for individuals to embrace efficacious preventive measures to mitigate the disease burden stemming from norovirus infections.

References

Fan Ping, Wang Ermei, Chen Baolin. (2023). Analysis of Norovirus Infection in Patients with Foodborne Diseases in Sentinel Hospitals in Changzhou City from 2016 to 2020. *Chinese Journal of Viral Diseases, 13*(1), pp. 67-71.

Ford-Siltz, Lauren A. Tohma, KentaroParra, Gabriel I. (2021). Understanding the relationship between norovirus diversity and immunity. *Gut Microbes, 13*(1), pp. 1-13.

He Fei, Shen Yongming. (2022). Research Progress on Norovirus. *Chinese Journal of Urban and Rural Enterprise Hygiene, 8*(8), pp. 41-43.

Hong Xiaojing, Xue Liang, Huang Dandan. (2022). Advances in Research on the Structure and Function of Norovirus Capsid Protein. *Modern Preventive Medicine, 49*(11), pp. 2097-2100.

Honglu Zhou, Songmei Wang, Lorenz von Seidlein. (2019). The epidemiology of norovirus gastroenteritis in China: disease burden and distribution of genotypes. *Frontiers of Medicine, 14*(1), pp. 1-7.

Jin Wenjun, Wang Ruiqin, Cai Xu. (2022). Epidemiological Characteristics of Norovirus Diarrhea Outbreaks in Changping District, Beijing from 2017 to 2020. *Capital Journal of Public Health, 16*(6), pp. 359-361.

Lang Zhongkai, Gan Yulu, Yan Zhaoyang. (2022). Epidemiological Characteristics of Norovirus Infection in Wanzhou District, Chongqing from 2015 to 2021. *Chinese Primary Health Care, 36*(11), pp. 91-94.

Lang Zhongkai, Tan Wenli, Gan Yulu. (2023). Epidemiological Characteristics of GII Norovirus in Wanzhou District, Chongqing. *Journal of Modern Medicine & Health, 39*(6), pp. 982-985.

Liao Yingyin, Xue Liang, Gao Junshan. (2021). Research Progress on Molecular Structure Characteristics of Norovirus and the Function of Its Capsid Protein. *Chinese Journal of Virology, 37*(2), pp. 459-463.

Na Wei, Jun Ge, Changyao Tan. (2021). Epidemiology and evolution of Norovirus in China. *Human Vaccines & Immunotherapeutics, 17*(11), pp. 4553-4566.

Natalie Winder, Sara Gohar and Munitta Muthana. (2022). Norovirus: An Overview

of Virology and Preventative Measures. *Viruses, 14*(12), pp. 1-21.

Preeti Chhabra, Miranda de Graaf, Gabriel I. Parra. (2019). Updated classification of norovirus genogroups and genotypes. *Journal of General Virology, 100*(10), pp. 1393-1406.

Robilotti, Elizabeth, Deresinski, Stan, Pinsky, Benjamin A. (2015). Norovirus. *Clinical Microbiology Reviews, 28*(1), pp. 134-164.

Shi Shuilang, Lv Lei, Duan Tianxiao. (2022). Epidemiological Characteristics of Norovirus Infection in Lin'an District, Hangzhou City from 2012 to 2020. *Shanghai Journal of Preventive Medicine, 34*(7), pp. 650-654.

Sun Zhiqiang, Huang Zhicheng, Wang Xiu. (2020). Research Progress on Norovirus Detection Technology. *Chinese Journal of Laboratory Diagnosis, 24*(10), pp. 1750-1752.

Wei Kaixin, Shi Anqi, Cao Yan. (2023). Epidemiological Characteristics and Pathology of Norovirus-Induced Infectious Diarrhea in Ningxia Region from 2019 to 2020. *Chinese Journal of Virology, 39*(1), pp. 96-103.

Wu Bingshan, Huang Zhimiao, Lin Weidong. (2023). Molecular Epidemiological Characteristics of GII Norovirus in Children Under 5 Years Old in Fuzhou City from 2016 to 2021. *Chinese Journal of Zoonoses, 39*(5), pp. 471-477.

Yao Xin, Liang Zhenglun. (2018). Research Progress on the Structure and Evolution of Norovirus. *Chinese Journal of Viral Diseases, 8*(1), pp. 72-76.

Zhang Chao, Deng Jianjun, Zhang Ruijuan. (2017). Advances in Molecular Biology Research on Norovirus. *Chinese Preventive Medicine, 18*(1), pp. 49-53.

Zhao Ji. (2018). Decrypting Norovirus. *Biology Teaching, 43*(3), pp. 63-64.

Zhao Jingjing, Wang Jiajia, Xiao Guiyong. (2023). Epidemiological Characteristics of Norovirus Diarrhea in Fengtai District, Beijing from 2017 to 2021. *Chinese Journal of Virology, 39*(1), pp. 125-130.

Zheng Yan, Cui Lihong. (2016). Molecular Biology Progress of Norovirus. *Chinese Journal of Gastroenterology and Hepatology, 25*(12), pp. 1475-1480.