Vital Surveillances

An Increasing Prevalence of Non-GII.4 Genotypes Causing Norovirus Gastroenteritis Outbreaks — Beijing Municipality, China, 2017–2024

Hongbo Jing[1]; Yanhui Yang[2]; Mu He[1]; Yanbo Wang[1]; Yu Zhao[1]; Zhan Li[1]; He Zhang[1]; Nan Jia[1]; Yanmeng Gao[1]; Shengtian Liu[1]; Tao Peng[1,#]; Miao Jin[2,#]

ABSTRACT

Objectives: Since 2014, non-GII.4 norovirus genotypes have increasingly challenged the predominance of GII.4, particularly in Asia. This study analyzed the epidemiological and genetic characteristics of norovirus outbreaks from January 2017 to June 2024 in a district of Beijing, China.

Methods: We tested 2,016 stool samples collected from 309 acute gastroenteritis outbreaks for norovirus using real-time RT-PCR. Partial polymerase and capsid sequences of norovirus-positive samples were amplified and sequenced for phylogenetic analysis. Additionally, we performed genome amplification and sequence analysis on seven GII.7[P7] strains.

Results: Between January 2017 and June 2024, 150 norovirus outbreaks were reported, with GII norovirus causing 83.3% of these outbreaks. We identified 16 distinct genotypes. Among the 102 GII genotype outbreaks, non-GII.4 norovirus outbreaks (81.4%) significantly outnumbered GII.4 norovirus outbreaks (18.6%). The three most prevalent genotypes during the study period were GII.2[P16] (46.1%, 47/102), GII.3[P12] (14.7%, 15/102), and GII.4 Sydney[P16] (12.7%, 13/102). GII.2[P16] predominated in 2017, 2018, and 2020, while GII.3[P12] was the dominant genotype in 2022. Multiple genotypes emerged in 2023. In the first half of 2024, GII.4 Sydney[P16] became predominant (36.9%), while a novel GII.7[P7] variant emerged, accounting for 26.3% of outbreaks. All seven GII.7[P7] genome sequences formed an independent branch in both VP1 and polymerase regions.

Conclusions: Our findings demonstrate that non-GII.4 noroviruses play an increasingly important role in outbreaks in Beijing. Continuous surveillance is needed to better understand and control norovirus outbreaks in future epidemic seasons.

Norovirus (NoV) is one of the leading pathogens causing outbreaks of acute gastroenteritis (AGE). NoV is a single-stranded RNA virus with a highly diverse genome that can be classified into 10 genogroups (GI to GX). Among these, GI and GII are the most common genotypes causing AGE and are further divided into 9 GI and 27 GII genotypes based on amino acid sequences of the complete viral protein 1 (VP1), while 14 GI and 37 GII P types have been identified based on partial nucleotide sequences of the RNA-dependent RNA polymerase (RdRp) regions (*1*).

The GII.4 norovirus has been the predominant genotype in global epidemics, with novel pandemic GII.4 variants emerging approximately every 2–3 years since the mid-1990s, including GII.4 US95/96, Farmington Hills 2002, Hunter 2004, Den Haag 2006, New Orleans 2009, and Sydney 2012 (*2*). However, since 2014, novel non-GII.4 genotypes have emerged as the primary cause of outbreaks, surpassing GII.4 in China and other countries, including GII.17 in the winter season of 2014–2015 and GII.2[P16] in 2016–2017 (*3*–*5*).

Since February 2017, a significant increase in AGE outbreaks has been observed in a district of Beijing. To better understand the genetic variation of norovirus causing these recent acute gastroenteritis outbreaks, we analyzed the genetic characteristics of norovirus detected from AGE outbreaks during 2017–2024.

METHODS

Source of Specimens

Fecal specimens or anal swabs were collected from AGE cases in a district of Beijing from 2017 to 2024. AGE was defined as three or more episodes of diarrhea and/or two episodes of vomiting within 24 hours. A norovirus outbreak was defined as three or more AGE

cases occurring in the same location within three days, with at least two laboratory-confirmed NoV cases (*6*).

Genotyping and Sequence Analysis

NoV detection and genotyping were performed on positive samples using previously described protocols (*7*). Genotypes were determined using the Norovirus Typing Tool (http://www.rivm.nl/mpf/norovirus/typingtool). The complete RdRp and VP1 genomic fragments of GII.7[P7] (Supplementary Table S1, available at https://weekly.chinacdc.cn/) were amplified. Nucleotide sequence alignment was performed using MEGA v5.0. The optimal nucleotide substitution models for Bayesian evolutionary analysis of the GII.7 VP1 (1,623 bp) and RdRp (1,530 bp) coding genes were determined using PhyloSuite v1.2.2. Parameter settings were configured in BEAUti v1.10.4, and path sampling was employed to identify the best combination of molecular clock and population growth models. The reliability of posterior results was assessed using Tracer v1.7.2, with convergence considered achieved when all parameters had an ESS (Effective Sample Size) >200. The maximum clade credibility tree was constructed using TreeAnnotator v1.10.4, and phylogenetic tree visualization was enhanced using the Chiplot website. Validation in BEAST v1.10.4 confirmed that the strict molecular clock model and constant population growth model were applied for the evolutionary analysis of VP1 (HKY) and RdRp (GTR). Reference sequences for NoV were obtained from the GenBank database. The χ^2 test was used to compare differences among strains, with significance assumed at $P<0.05$. All statistical analyses were performed using IBM SPSS Statistics 25.0.

RESULTS

Epidemiological Distribution of NoV Outbreaks

Between January 2017 and June 2024, a total of 309 acute gastroenteritis outbreaks occurred in a district of Beijing, China, of which 150 (48.5%) were laboratory-confirmed as norovirus. GII was the predominant genogroup (125/150, 83.3%), followed by GI (23/150, 15.3%) and multiple genotypes (2/150, 1.3%). Two significant seasonal peaks were observed during March-April and November-December each year (Figure 1). Schools were the most frequent outbreak setting (145/150, 96.7%), including primary schools (68/145, 46.9%), kindergartens (61/145, 42.1%), middle schools (14/145, 9.6%), and universities (2/145, 1.4%). Person-to-person transmission was reported in 98.0% (147/150) of outbreaks, while foodborne transmission accounted for only 2.0% (3/150).

Genotype Distribution

Of 895 NoV-positive samples confirmed by real-time RT-PCR, 796 samples from 117 outbreaks were successfully genotyped by sequencing. Fifteen GI outbreaks were identified, comprising six genotypes: GI.6[P11] (4/15), GI.3[P13] (4/15), GI.5[P4] (3/15),

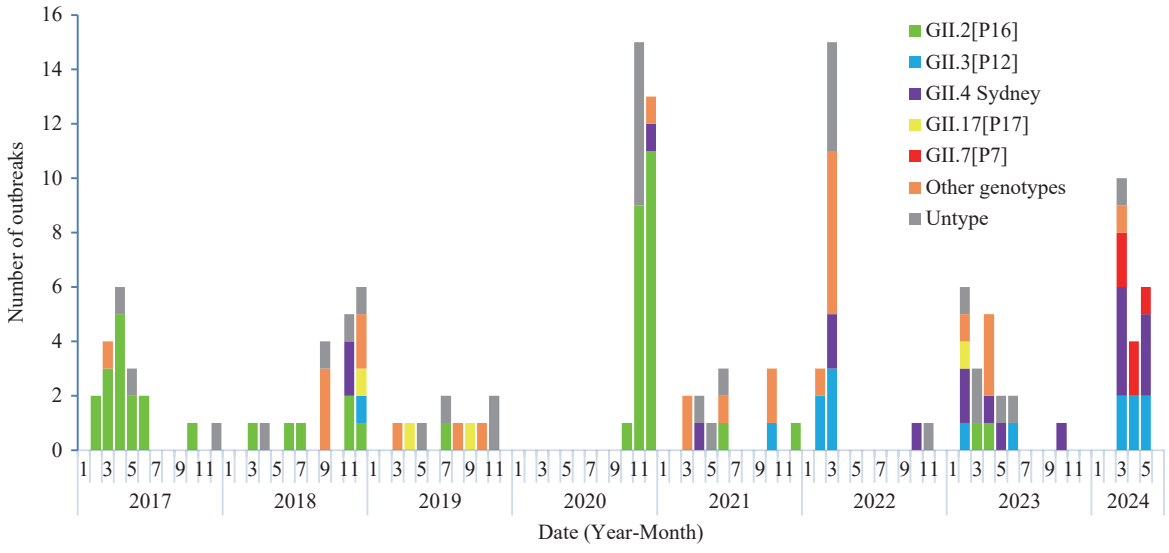

FIGURE 1. Genotype distribution of norovirus (NoV) outbreaks according to time from 2017 to 2024.

GI.4[P4] (2/15), GI.6[P6] (1/15), and GI.2[P2] (1/15). Among the 102 GII outbreaks, ten genotypes were identified, with non-GII.4 NoV outbreaks (83/102, 81.4%) significantly outnumbering GII.4 NoV outbreaks (19/102, 18.6%). The three most prevalent genotypes during the study period were GII.2[P16] (47/102, 46.1%), GII.3[P12] (15/102, 14.7%), and GII.4 Sydney[P16] (13/102, 12.7%). GII.2[P16] was the predominant genotype in 2017, 2018, and 2020, responsible for 100% (15/15), 54.5% (6/11), and 91.3% (21/23) of the GII outbreaks, respectively. GII.3[P12] was predominant in 2022 (5/9, 55.6%) and the second most prevalent genotype in the first half of 2024 (6/19, 31.6%). Among GII.4 Sydney variants, GII.4 Sydney[P16] was predominant only in the first half of 2024 (7/19, 36.8%), while GII.4 Sydney[P31] caused only 6 outbreaks throughout the entire study period. No clear predominant genotype was observed in 2019, 2021, and 2023. Notably, a novel GII.7[P7] strain was detected for the first time in March 2024, accounting for 26.3% (5/19) of GII outbreaks in Beijing during the first half of 2024 (Figure 1).

Among the GII genotyped outbreaks, GII.2[P16] was associated with the widest range of outbreak settings, primarily occurring in kindergartens and primary schools (87.2%, 41/47). In contrast, GII.3[P12] and GII.7[P7] were exclusively detected in kindergartens and primary schools. GII.17[P17] outbreaks were limited to primary and middle schools, while GII.4 Sydney affected kindergartens, primary schools, and middle schools (Table 1). Several other GII genotypes caused ≤5 outbreaks throughout the study period, including GIX.1[GII.P15] (n=1), GII.12[P16] (n=2), GII.17[P17] (n=4), GII.8[P8] (n=4), and GII.6[P7] (n=5).

Information on patient age was available for 796 patients from 117 genotyped outbreaks. The proportion of male patients was significantly higher than female patients, with gender distributions differing significantly among NoV strains (P<0.05) (Table 2). The median age of affected cases was 8 years. The proportion of patients ≤5 years of age was higher for GII.4 Sydney (69.0%) and GII.7[P7] (65.2%), while GII.2[P16] and GII.3[P12] had higher proportions in the 6–9 years group. GII.17[P17] was more likely to be observed in cases 10–18 years of age (65.7%). The age distributions differed significantly among NoV strains (P<0.05) (Table 2).

TABLE 1. Genotype distribution of norovirus (NoV) outbreaks from 2017 to 2024 according to setting.

Setting	No. outbreaks of norovirus					
	GII.2[P16]	GII.3[P12]	GII.4 Sydney	GII.7[P7]	GII.17[P17]	Other genotypes
Kindergartens	19	9	14	2	0	17
Primary schools	22	6	3	3	3	31
Middle schools	4	0	2	0	1	7
Universities	1	0	0	0	0	1
Other	1	0	0	0	0	4
Total	47	15	19	5	4	60

TABLE 2. Genotype distribution of norovirus (NoV) outbreaks from 2017 to 2024 according to age and sex.

Characteristics	Total	Patients linked to outbreaks of norovirus [n (%)]							
		GII.2[P16]	GII.3[P12]	GII.4 Sydney	GII.7[P7]	GII.17[P17]	Other genotypes	X^2	P
Sex								12.65	<0.05
Male	462 (58.0)	199 (52.4)	45 (69.2)	57 (67.9)	15 (65.2)	22 (62.8)	124 (59.1)		
Female	334 (42.0)	181 (47.6)	20 (30.8)	27 (32.1)	8 (34.8)	13 (37.1)	85 (40.9)		
Age (year)								200.85	<0.05
0–5	231 (29.0)	99 (26.1)	24 (36.9)	58 (69.0)	15 (65.2)	0	35 (16.7)		
6–9	264 (33.2)	140 (36.8)	29 (44.6)	18 (21.4)	4 (17.4)	10 (28.6)	63 (30.1)		
10–18	180 (22.6)	95 (25)	12 (18.5)	4 (4.8)	4 (17.4)	23 (65.7)	42 (20.1)		
>19	121 (15.2)	46 (12.1)	0	4 (4.8)	0	2 (5.7)	69 (33.1)		
Total	796 (100.0)	380 (100.0)	65 (100.0)	84 (100.0)	23 (100.0)	35 (100.0)	209 (100.0)		

The Genome Analysis of the Novel GII.7[P7]

We analyzed 7 full VP1 genome sequences from this study alongside reference sequences from GenBank to generate time-scaled evolutionary trees for both VP1 and RdRp regions. Four distinct clusters of GII.7 strains were identified: GII.7(1990–2003), GII.7(2004–2009), GII.7(2008–2017), and GII.7(2015–2024). The GII.7(2015–2024) cluster contained two subclusters (SC): SC1 comprised two strains from Paraguay (MW305562) and the United Kingdom (MH218661) from the 2015/16 season, while SC2 consisted of all seven GII.7[P7] strains from our study, together with a Russian-2024 strain (PQ100948) (Figure 2A). In the RdRp region, all GII.P7 RdRp sequences grouped within cluster IV, which contained three sublineages (a–c). All 7 GII.7[P7] strains from our study, along with the Russian-2024 strain, formed sublineage 2 and were closely related to strains from Paraguay and the United Kingdom (sublineage 1) (Figure 2B).

DISCUSSION

In 2017, our laboratory joined the national norovirus outbreak laboratory network (CaliciNet China) and became one of the network laboratories in China (*8*). This study identified two significant seasonal peaks of norovirus outbreaks occurring in March-April and November-December, consistent with previous reports that norovirus outbreaks in the northern hemisphere, including China, generally peak from November to March of the following year (*9*). Norovirus outbreaks in this study primarily affected kindergartens and primary schools, with children under 12 years of age emerging as the most susceptible population, similar to findings from other regions of China (*8*). In contrast, in Western countries such as the United States and Norway, norovirus outbreaks predominantly occur in long-term care facilities (LTCF) and among people aged ≥65 years (*10*). These inconsistencies may be attributed to significant differences in the sensitivity and coverage of regional surveillance systems across different countries.

Since 2012, GII.4 Sydney has been the predominant norovirus genotype worldwide (*3*), existing as two types: GII.4 Sydney[P31] and GII.4 Sydney[P16]. These two genotypes have consistently been the predominant strains in both outbreaks and sporadic cases of AGE in many countries. However, novel non-GII.4 genotypes have been increasingly documented, particularly GII.17[P17] in the winter season of 2014-2015 and GII.2[P16] in 2016–2017, causing increased NoV outbreaks in China and other countries (*3*–*5*). In this study, while GII.4 Sydney[P16] only showed a significant increase in the first half of 2024, 93.75% of norovirus outbreaks in 2017 were caused by GII.2[P16], peaking in April. This pattern was consistent with the general trend observed throughout Beijing (*6*). No norovirus outbreaks occurred from January to September 2020 due to the implementation of home-based online classes during the COVID-19 pandemic. Norovirus outbreaks increased sharply after November 2020, with GII.2[P16] remaining the predominant genotype, a finding also observed in national surveillance data (*9*). Ao et al. analyzed the transmission of GII.2[P16] norovirus during the winter of 2016–2017 in China and found that it originated in Guangdong in late 2016 before spreading northward in 2017 (*11*), subsequently becoming the dominant genotype in norovirus outbreaks across China from 2016 to 2020 (*9*). According to Jin et al., GII.3[P12] primarily affected children, while GII.17[P17] outbreaks tended to infect older children and adults in China (*8*). These findings revealed that the median age of susceptible individuals varied depending on the norovirus genotype. GII.3[P12] was the second most common genotype in our study, with most strains detected in children under 9 years of age from 2022 to 2024. Phylogenetic analysis shows the evolution of GII.3[P12] norovirus in chronological order, which may be attributed to antigenic drift of the GII.3 VP1 protein and intergenic recombination (*12*).

In this study, a non-GII.4 genotype, GII.7[P7], drew our attention as it became a predominant genotype (26.3%), causing norovirus outbreaks during the first half of 2024. GII.7[P7] formed an independent branch in the phylogenetic tree, indicating that the GII.7[P7] strain in this study represents a novel GII.7 variant. The majority of surveillance data has shown that the detection rate of GII.7 typically ranges from <1% to 7% (*13*). In our study, GII.7[P7] infections were predominantly observed in children under 5 years old. Previous data from Australian norovirus outbreak monitoring showed that the median age of GII.7[P7] patients was 39 years (range: 1–89 years). Recently, a metagenomic study conducted in nine infants (aged 2 weeks to 12 months) from Mexico found that three infants were infected by GII.7[P7] (*14*). These data suggest that GII.7[P7] affects individuals across a wide age range.

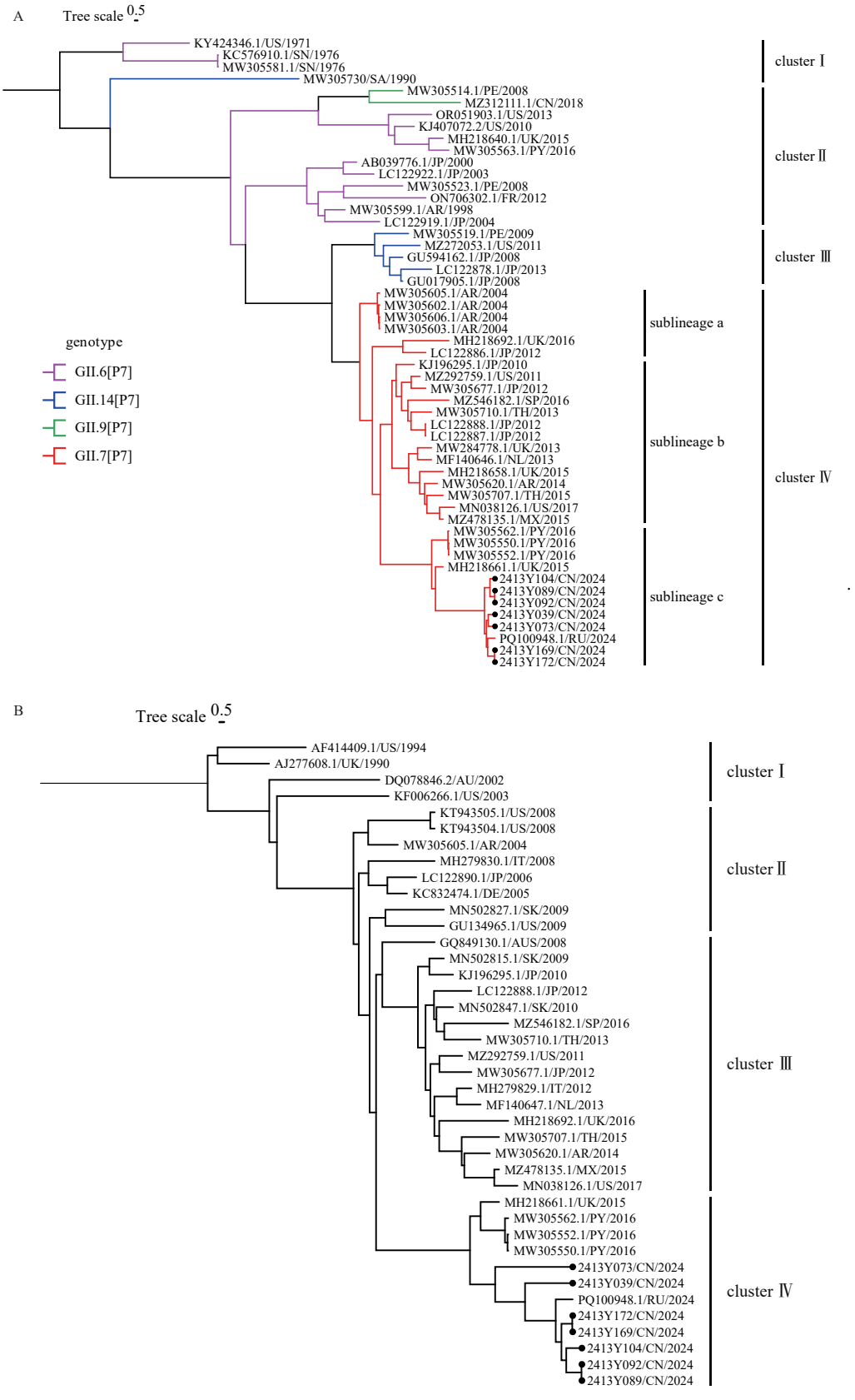

FIGURE 2. Phylogenetic analysis based on RdRp (1,530 bp) and VP1 (1,623 bp) gene of GII.7[P7]. (A) Phylogenetic tree for RdRp region; (B) Phylogenetic tree for GII VP1 region.
Note: Norovirus strains detected in this study were marked with the following symbols: ●.

In conclusion, we analyzed the epidemiological and genetic features of NoV outbreaks from January 2017 to June 2024 in Beijing. We observed significant changes in the predominant genotypes over time: GII.2[P16] was predominant in both 2017 and 2020, GII.3[P12] in 2022, multiple genotypes in 2023, and a novel GII.7[P7] variant in the first half of 2024. Further work to assess the spread of these genotypes and determine any differences in clinical severity or impact should be prioritized alongside molecular characterization as we approach the winter months.

Conflicts of interest: No conflicts of interest.

Funding: Supported by High-level Public Health Technology Talent Construction Project: Discipline Backbone- 01-026.

doi: 10.46234/ccdcw2025.129

[#] Corresponding authors: Tao Peng, pt16@tsinghua.org.cn; Miao Jin, jinmiao@ivdc.chinacdc.cn.

[1] Shunyi District Center for Disease Control and Prevention, Beijing, China; [2] National Institute for Viral Disease Control and Prevention, Chinese Center for Disease Control and Prevention, Beijing, China.

Submitted: December 27, 2024
Accepted: May 22, 2025
Issued: June 06, 2025

REFERENCES

1. Chhabra P, de Graaf M, Parra GI, Chan MCW, Green K, Martella V, et al. Updated classification of norovirus genogroups and genotypes. J Gen Virol 2019;100(10):1393 – 406. https://doi.org/10.1099/jgv.0.001318.
2. Vinjé J. Advances in laboratory methods for detection and typing of norovirus. J Clin Microbiol 2015;53(2):373 – 81. https://doi.org/10.1128/jcm.01535-14.
3. Jin M, Zhou YK, Xie HP, Fu JG, He YQ, Zhang S, et al. Characterization of the new GII. 17 norovirus variant that emerged recently as the predominant strain in China. J Gen Virol 2016;97(10):2620 – 32. https://doi.org/10.1099/jgv.0.000582.
4. Kwok K, Niendorf S, Lee N, Hung TN, Chan LY, Jacobsen S, et al. Increased detection of emergent recombinant norovirus GII.P16-GII.2 strains in young adults, Hong Kong, China, 2016-2017. Emerg Infect Dis 2017;23(11):1852-5. http://dx.doi.org/10.3201/eid2311.170561.
5. Bidalot M, Théry L, Kaplon J, De Rougemont A, Ambert-Balay K. Emergence of new recombinant noroviruses GII.p16-GII.4 and GII.p16-GII.2, France, winter 2016 to 2017. Euro Surveill 2017;22(15):30508. http://dx.doi.org/10.2807/1560-7917.ES.2017.22.15.30508.
6. Gao ZY, Liu BW, Yan HQ, Li WH, Jia L, Tian Y, et al. Norovirus outbreaks in Beijing, China, from 2014 to 2017. J Infect 2019;79(2):159 – 66. https://doi.org/10.1016/j.jinf.2019.05.019.
7. Cannon JL, Barclay L, Collins NR, Wikswo ME, Castro CJ, Magana LC, et al. Genetic and epidemiologic trends of norovirus outbreaks in the United States from 2013 to 2016 demonstrated emergence of novel GII. 4 recombinant viruses. J Clin Microbiol 2017;55(7):2208 – 21. https://doi.org/10.1128/JCM.00455-17.
8. Jin M, Wu SY, Kong XY, Xie HP, Fu JG, He YQ, et al. Norovirus outbreak surveillance, China, 2016-2018. Emerg Infect Dis 2020;26(3):437 – 45. https://doi.org/10.3201/eid2603.191183.
9. Zhu X, He YQ, Wei XY, Kong XY, Zhang Q, Li JX, et al. Molecular epidemiological characteristics of gastroenteritis outbreaks caused by norovirus GII.4 sydney [P31] strains - China, October 2016-December 2020. China CDC Wkly 2021;3(53):1127-32. http://dx.doi.org/10.46234/ccdcw2021.276.
10. Steele MK, Wikswo ME, Hall AJ, Koelle K, Handel A, Levy K, et al. Characterizing norovirus transmission from outbreak data, United States. Emerg Infect Dis 2020;26(8):1818 – 25. https://doi.org/10.3201/eid2608.191537.
11. Ao YY, Cong X, Jin M, Sun XM, Wei XM, Wang JJ, et al. Genetic analysis of reemerging GII.P16-GII.2 noroviruses in 2016-2017 in China. J Infect Dis 2018;218(1):133-43. http://dx.doi.org/10.1093/infdis/jiy182.
12. Mahar JE, Bok K, Green KY, Kirkwood CD. The importance of intergenic recombination in norovirus GII. 3 evolution. J Virol 2013;87(7):3687 – 98. https://doi.org/10.1128/JVI.03056-12.
13. Bruggink LD, Moselen JM, Marshall JA. The comparative molecular epidemiology of GII.P7_GII.6 and GII.P7_GII.7 norovirus outbreaks in Victoria, Australia, 2012-2014. Intervirology 2016;59(1):60-5. http://dx.doi.org/10.1159/000448100.
14. Rivera-Gutiérrez X, Morán P, Taboada B, Serrano-Vázquez A, Iša P, Rojas-Velázquez L, et al. High prevalence and diversity of caliciviruses in a community setting determined by a metagenomic approach. Microbiol Spectr 2022;10(1):e0185321. https://doi.org/10.1128/spectrum.01853-21.

SUPPLEMENTARY MATERIAL

SUPPLEMENTARY TABLE S1. Primers used for amplification of the complete genomic fragment of GII.7[P7] in this study.

Primers	Sequence (5'–3')	Size (bp)	Start Positions*
GII.7[P7]-ORF1_1-F	CTAACAAAGAAGAGGTTGGTG	1,296	49
GII.7[P7]-ORF1_1-R	GTGAAGATGATTTAGTGGACAG		1323
GII.7[P7]-ORF1_2-F	GTGTAAAGACCTAGGGAACTAC	1,154	1094
GII.7[P7]-ORF1_2-R	CACACTCATTGAATTTCACAT		2227
GII.7[P7]-ORF1_3-F	TGACAAAAATGGCAATACCC	1,200	1952
GII.7[P7]-ORF1_3-R	AACTCTCCAGACTTATGAACTTG		3129
GII.7[P7]-ORF1_4-F	GTCACTGGCTCAGACATCA	1,164	2877
GII.7[P7]-ORF1_4-R	AACAAGCTCATCTTTAAGCG		4021
GII.7[P7]-ORF1_5-F	AGGAAGCAAAGAAGACAGTG	1,141	3781
GII.7[P7]-ORF1_5-R	TTGATGACCATCTTGCTAACTTT		4899
GII.7[P7]-ORF2_1-F	GGCCTGATAAAACTGAAGGC	1,259	4541
GII.7[P7]-ORF2_1-R	TGCTGTGTACATCATTTCCAC		5779
GII.7[P7]-ORF2_2-F	AATTTCTTCCATTACAATCAGGG	1,164	5533
GII.7[P7]-ORF2_2-R	CCCCAGCATTTATGAGTGAA		6676
GII.7[P7]-ORF3-F	CCAACACTTCTATCAAGAAGC	1,031	6417
GII.7[P7]-ORF3-R	TCTTTTCACTAAATCTGTGACTCC		7424

* The start position in strain Arg4416 (accession No: MW305606).