Original Article

Epidemiological Survey and Analysis on an Outbreak of Gastroenteritis due to Water Contamination*

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Abstract

Objective To document the investigation and control of an outbreak of gastroenteritis in City G, South China, and provide a reference for preventing future outbreaks.

Methods An ambispective cohort study was designed. Attack rate (AR) and relative risks (RR) were calculated to identify the causes of gastroenteritis. Investigations using questionnaires included personal interviews with patients and doctors, reviews of medical records, laboratory examinations of fecal specimens and continuous hygiene monitoring of water samples from the waterworks.

Results Overall, 427/71534 (AR=5.97‰) cases were identified between October 31 and November 12 2010. Geographic distribution was highly localized, with 80% of cases occurring in the areas supplied by waterworks-A. Consumption of water provided solely by waterworks-A was found to be associated with illness (RR=8.20, 95 CI%:6.12–10.99) compared with that from waterworks-B. Microbiological analyses confirmed the presence of Norovirus in six of eight fecal samples from symptomatic patients, two water samples from waterworks-A and two sewage samples. After taking effective measures, the hygienic indices of waterworks-A met health criteria again on November 9 and no cases were reported 3 days later.

Conclusion The outbreak reported here was caused by drinking tap water contaminated with sewage at the source. Early identification of possible contamination sources and awareness of changes that might negatively impact water quality are important preventive measures to protect public health.

Key words: Water contamination; Norovirus; Outbreak; Survey and analysis

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INTRODUCTION

Between October 31 and November 12, 2010 an outbreak of acute gastroenteritis occurred in Town C, City G, South China. The outbreak was highly localized, with more than 80% of cases clustered in waterworks-A supply areas. A cohort study confirmed an association between illness and consumption of drinking water from waterworks-A. Microbiological analyses detected Norovirus in patient stool samples and water samples from both the delivery point and the terminal point of the pipe network of waterworks-A. On the basis of epidemiological surveys and microbiological findings, the outbreak was determined to have been caused by waterborne Norovirus originating from water source contamination.

The reported census population for Town C is 71

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534 distributed in 17 villages, living mainly on local agriculture, industry and business. There are six primary schools, two middle schools, one college, and one hospital in the town. Drinking water is supplied from two central water supply systems located within Town C: A and B. The source for both waterworks is River L, which flows through the town.

Doctors in the hospital found the number of alimentary tract cases increased abnormally from October 31 and reported this to the local Center for Disease Control (CDC) on November 5. The local CDC began to investigate immediately and continued until the end of the outbreak. In view of the high attack rate, the local CDC implemented relative control measures, and an ambispective cohort study was launched to determine the causes and transmission routes of the outbreak. Investigations with questionnaires included personal interviews of patients and doctors, reviews of medical records, laboratory examinations of fecal specimens and continuous hygiene monitoring of water samples from the waterworks. With the microbiological confirmation of Norovirus in both patients' stool samples and water samples from the delivery point or pipe network terminal point, more targeted control measures were implemented and the outbreak was effectively controlled. Here we share our experiences with all of our colleagues.

MATERIALS AND METHODS

Epidemiological Investigation

A brief and standardized questionnaire addressing the actual condition was designed based on the "Individual case questionnaire form of acute gastroenteritis outbreak caused by Norovirus" published by the China CDC[1]. The study was approved by the Institutional Review Board of the Guangzhou CDC. After obtaining informed consent, investigations were conducted by experienced professionals through reviewing medical records of out-patient departments and interviewing doctors and patients. River L flow data and water supply information from the waterworks were collected to determine the etiological agent and mode of transmission using environmental-epidemiological analysis.

Case Definition

Case definition was established according to the "Guidelines for prevention and control of infectious diarrhea caused by Norovirus in Guangdong province"[2]. A case of gastroenteritis was defined as any person working or residing in Town C who had an episode of acute diarrhea (defined as three or more loose/liquid stools within a 24-h period), or defecated less than three times but with modification of stool characteristics and vomiting, or vomiting as the major symptom, or two or more of the following signs: fever, abdominal pain, malaise and nausea on or after October 31, 2010, to the end of the epidemic.

Laboratory Investigation

From November 6 to 11, 2010, routine testing (Physical and Chemical: the concentration of chlorine dioxide, ammonia nitrogen, mercury, aluminum, and arsenic et al.; Microbiological: counts of total bacteria, total coliforms and heat-resistant coliforms) of the source, delivery and pipe network terminal point water from waterworks was performed according to the "Standard examination methods for drinking water" (GB/T 5750-2006)[3]. Following notification of the results, water sampling and concentration procedures were additionally conducted. Viruses from the water samples were precipitated with 16% PEG8000-0.525 mol/L NaCl[4].

Fecal samples and anal swabs were collected from patients who had current gastrointestinal symptoms without antibiotic treatment and sent to the laboratory of Guangzhou CDC for routine testing for the presence of pathogenic bacteria including *Salmonella* sp., *Shigella* sp., *Vibrio parahemolyticus*, *Vibrio cholerae*, *Escherichia coli*, and *Staphylococcus aureus* according to "Diagnostic criteria for infectious diarrhea" (WS271-2007)[5].

Subsequently, as viral origin was suspected in this outbreak, One-step PrimeScript™ real-time RT-PCR Kit (Takara, Japan) and ELISA test (RIDASCREEN®, Germany) were used for the identification of Norovirus according to the manufacturer's instructions. The primer sets and probe for real-time RT-PCR were:

NVF: 5'-CAAGAGCCKATGTTCAGATGGATGAG-3';
NVR: 5'-TCGRCGCCATCTTCATTCACA-3';
NVP: 5'-FAM-TGGGAGGGCGATCGCAATCTG- BHQ1-3';

The conditions for one-step RT-PCR consisted of RT for 30 min at 50 °C followed by Taq activation at 95 °C for 3 min then 40 PCR cycles of 95 °C for 15 s and 60 °C for 1 min, as recommended by the manufacturer. The ABI Prism 7 500 sequence detector was used to analyze the emitted fluorescence during amplification. The PCR products from stool and water samples were further characterized by sequencing alignment and phylogenetic analysis.

Cohort Study Design

An ambispective cohort study was conducted that included all residents in the villages where the drinking water was provided solely by waterworks-A or waterworks-B. The observation period covered 21 days, from October 26 to November 15, 2010. People who began present in the village after November 15 or those who were not present for the entire period of 21 days were excluded from the study. All subjects were informed of the risk of acute gastroenteritis and were retrospectively or prospectively interviewed on the development of gastroenteritis with the brief and standardized questionnaire.

Statistical Analysis

In addition to common statistical methods to describe the variables related to personal data, Chi-square test or Fisher's exact test for categorical variables were also performed to explore the potential risk factors. The attack rate (AR) and the relative risks (RR) due to exposure were calculated with their respective 95% confidence interval (CI). Statistical significance was determined using a *P* value <0.05. All analyses were carried out using the software package SPSS for Windows ver. 11.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

Descriptive Temporal Analysis

The outbreak began on October 31 and lasted until November 12. The outbreak peaked on November 5 and 6 (89 and 76 cases, respectively) and decreased from November 6. The latest reported date of onset of symptoms was November 12 (one case). A total of 427 residents were identified as having gastrointestinal manifestations (Figure 1).

Gender Distribution

Of the 427 patients, 210 (49.18%) were male and 217 (50.82%) were female, corresponding to a sex ratio (males to females) of 1.03. However, there were no significant differences on AR according to sex [male: 5.74‰ (210/36559) *vs.* female: 6.20‰ (217/34975); χ^2=0.64, *P*>0.05].

Age Distribution

All age groups were affected by the epidemic. The age-specific AR was highest among those 1–5 year group, and lowest in the 6–15 year old age group, giving a significant difference among different age groups (χ^2=69.04, *P*<0.01) (Table 1).

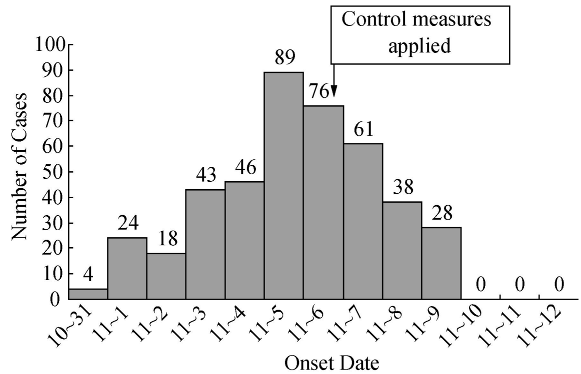

Figure 1. Epidemic curve of cases, by date of onset of symptoms, during an outbreak of gastroenteritisin town C, city G, South China, October 31 to November 15, 2010 (*n*=427).

Table 1. Age Distribution of Cases in Gastroenteritis Epidemic in Town C, City G

Age	Population	Number of Patients	Attack Rate (‰)
1–5	6847	70	10.23
6–15	10 066	14	1.39
16–25	19 855	107	5.39
26–40	17 551	124	7.07
40–65	14 101	101	7.16
≥65	3114	11	3.53
Total	71 534	427	5.97

Geographical Distribution

Table 2 and Figure 2 show the distribution of the total number of 427 gastroenteritis cases in the outbreak. Further analysis showed that the distribution in all the 17 villages in town C was significantly clustered in waterworks-A supply areas (e.g. Villages T1-T3, where drinking water was provided solely by waterworks-A, had 50 or more cases each). The total number of cases in villages T1-T5 where drinking water was partially or completely supplied by waterworks-A was 375, comprising 87.82% of all cases (Table 2).

Cohort Study

Among the 20 488 people living in the area where drinking water was provided completely by waterworks-A, 339 people were ill with an AR of 16.55‰.

Table 2. Location Distribution of Cases in Gastroenteritis Epidemic in Town C, City G

Village	Number of Patients	Constituent Ratio	Population	Attack Rate (‰)	Source of Water (Waterworks)
T1	225	52.69	10 024	22.45	A
T2	64	14.99	6402	10.00	A
T3	50	11.71	4062	12.31	A
T4	21	4.92	3974	5.28	A+B
T5	15	3.51	2290	6.55	A+B
T6	9	2.11	4288	2.10	B
T7	8	1.87	3274	2.44	B
T8	7	1.64	2704	2.59	B
T9	6	1.41	2652	2.26	B
T10	5	1.17	2820	1.77	B
T11	5	1.17	6492	0.77	B
T12	3	0.70	2474	1.21	B
T13	3	0.70	4292	0.70	B
T14	2	0.47	5848	0.34	B
T15	2	0.47	2802	0.71	B
T16	1	0.23	4606	0.22	B
T17	1	0.23	2530	0.40	B
Total	427	100.00	71 534	5.97	—

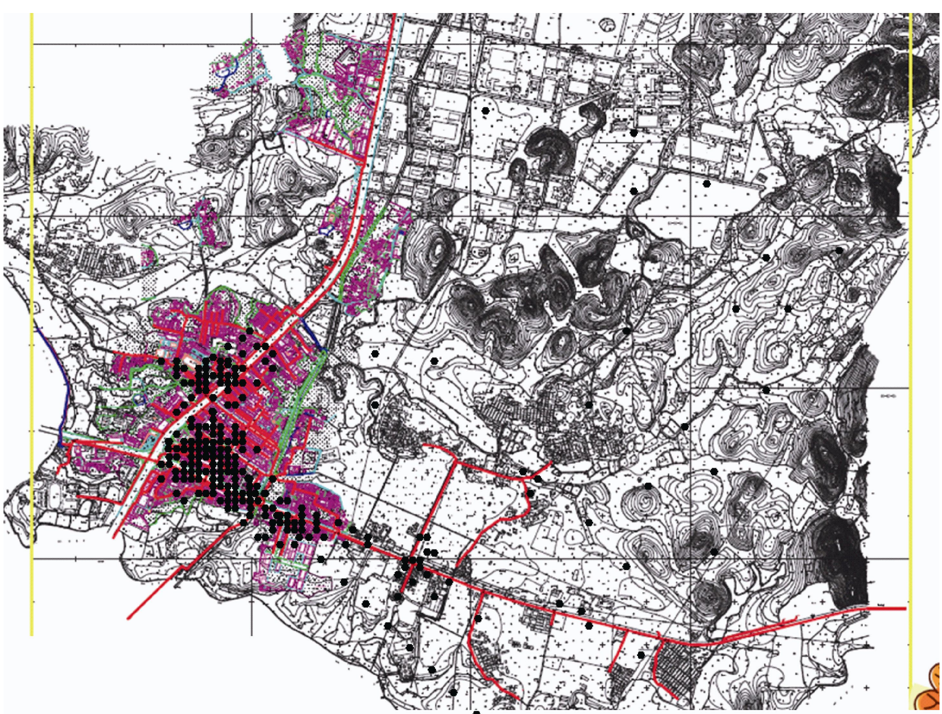

Figure 2. The distribution of gastroenteritis cases and water pipe network in town C city G. Red lines show the pipe network of waterworks A, the other area was supplied by waterworks B. Black dots (·) show the location of gastroenteritis cases.

In contrast, among the 44 782 people who drank only the water from waterworks-B, only 52 people were ill, giving an AR of 1.16‰. Thus, the risk of illness following consumption of tap water was significantly higher among those who drank the water from waterworks-A compared with those who drank the water from waterworks-B (RR=8.20, 95% CI:6.12–10.99) (Table 3).

Table 3. Cohort Analysis of Gastroenteritis Epidemic in Town C, City G

	Water Supplied Solely by Waterworks A	Water Supplied Solely by Waterworks B	Subtotal	Chi-Square Value	*P*-value	RR	95% CI
Illness	339	52	391				
Non-illness	20 149	44 730	64 879	282.13	0.00	8.20	6.12–10.99
Total	20 488	44 782	65 270				

Survey of Drinking Water

Waterworks-A supplied water to all people in T3-T4 villages and in part to T4-T5 villages. This waterworks utilized conventional sterilization procedures, such as coagulating sedimentation, filtration and disinfection. The main ingredient of disinfectant was chlorine dioxide, used before coagulating and twice before leaving waterworks. Surveillance found that there were many deficiencies including obsolete disinfectant devices and pipelines, thick dirt on the walls of the desilter and filtering ponds, low technology, an absence of health management systems and testing personnel, irregular management, and a shortage of water quality surveillance. Furthermore, a large drain outlet was located 70 meters downstream from the source of waterworks-A. The sewage discharged directly to the river without treatment because of the malfunction of a lift pumping station in the sewage treatment plant from October 1, 2010. The water around the drain outlet was yellow, muddy and smelly. Villagers who drank water from waterworks-A also complained that the water was muddy and smelly during November 1-4, 2010.

Waterworks-B supplied water to part of the population in villages T4-T5 and all of the population in T6-T17. Water sterilization procedures were similar to waterworks-A. However, waterworks B adopted new sterilizing equipment and the desilter and filtering ponds were clear. There were laboratory and lab workers to monitor indices routinely, including color, turbidity, smell, naked eye obvious inclusion, pH, total hardness, chlorine dioxide, total bacterial counts, and total coliform groups in water. With the exception of total bacterial counts and total coliform groups which were monitored daily, all other indices were tested twice per day. The water intake point of waterworks-B' was located 8 km upstream from waterworks-A' (Figure 3).

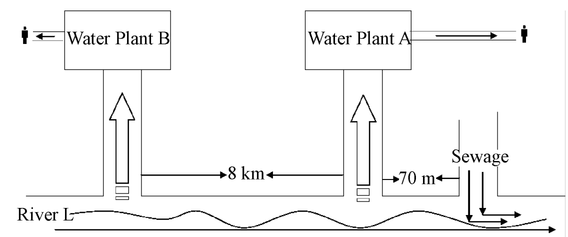

Figure 3. The location of water source of waterworks A and B.

Both waterworks A and B receive water from River L. The water flow of River L is usually 1 500 000 cubic meters per day but this decreased to 70 000 cubic meters per day from October 26 to November 3 because of an upstream closure. The number of gastroenteritis cases began to increase on the 6th day of its closure, and decreased again on the 3rd day after water flow returned to normal (Figure 4).

Laboratory Investigation of Clinical and Environmental Samples

We collected eight stool samples and nine anal swabs from 17 patients on November 6, 2010. None of the stool specimens and anal swabs from the patients was positive for bacterial culture including *Salmonella* sp., *Shigella* sp., *Vibrio parahemolyticus*, *Vibrio cholerae*, *Escherichia coli* and *Staphylococcus aureus*. Noroviruses were detected from six stool samples using Norovirus RT-PCR, among them two were positive by ELISA.

With the exception of the ammonia nitrogen index of waterworks-B (0.53mg/L), all other physical and chemical indices of source water met the class II standard of “environmental quality criteria for surface water”(GB3838-2002). For delivery water and pipe network terminal point water, most indices met the “criteria for living and drinking water”(GB5749-2006), except the aluminum in the delivery water(0.221mg/L) and aluminum(0.221mg/L) and arsenic(0.017mg/L) in the pipe network terminal point water from waterworks-A.

All water samples were negative for pathogenic bacteria, such as *Vibrio cholerae*, *Salmonella typhi,* and *Salmonella paratyphi*, et al. However, routine testing of the water collected from waterworks-A on November 6-8 showed positive results for general bacteria, total coliforms and heat-resistant coliforms together with a low level of chlorine dioxide. Virological tests of samples from delivery water and pipe network terminal point water from waterworks-A, and sewage water taken on November 6 confirmed the presence of Norovirus. The amplified PCR products from stool and water samples were sequenced, and a phylogenetic analysis was performed. The Noroviruses detected in the fecal specimens from the outbreak cases and that from the water samples were indistinguishable by DNA sequencing, with 100% sequence homology. On and after November 9, inspections of both water supply systems did not show any abnormal results (Table 4, Table 5).

Measures and Effect

On November 4, the reservoir upstream began to release water to enhance the flow of River L. From November 6, continuous surveillance of the drinking water quality was performed. Professionals were sent to waterworks-A to be responsible for: water disinfection and purification; complete disinfection of filter material; the delivery network; water treatment ponds; water quality monitoring; and standardizing the management of waterworks. From November 9 the drinking water quality of waterworks-A met health criteria.

Public health education on preventing diarrhea caused by Norovirus was strengthened. Residents were taught to practice good habits of eating cooked food, drinking boiled water, and washing hands before preparing and eating foods

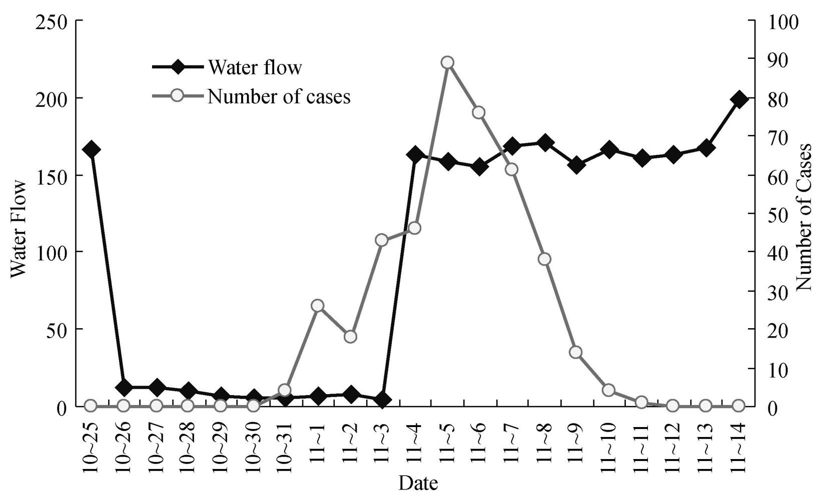

Figure 4. The relationship between variation of water flow and number of gastroenteritis cases in town C, city G.

Table 4. Results of Detection for Norovirus from Waterworks A and B

Sampling Point		Number of Samples	Result	
			November 6	**November 9**
Waterworks A	Source	1	negative	negative
	Delivery Point	1	**positive**	negative
	Pipe Network Terminal Point	1	**positive**	negative
Waterworks B	source	1	negative	negative
	Delivery Point	1	negative	negative
	Pipe Network Terminal Point	1	negative	negative
Drain Outlet		1	**positive**	**positive**

Table 5. Results of Microorganism and Chlorine Dioxide Detection from Waterworks A and B

Indices		Delivery Point Water				Pipe Network Terminal Point Water			
		Total Bacteria Count (CFU/mL)	Total Coliform (MPN/ 100 mL)	Heat-Resistant Coliform (MPN/ 100 mL)	Chlorine Dioxide (mg/L)	Total Bacteria Count (CFU/mL)	Total Coliform (MPN/ 100 mL)	Heat-Resistant Coliform (MPN/ 100 mL)	Chlorine Dioxide (mg/L)
Standard value		≤100	undetected	undetected	≥0.1	≤100	undetected	undetected	≥0.02
Water works A	November 6	740	undetected	undetected	0.05	1100	240	240	0.01
	November 7	330	2	undetected	0.08	800	300	120	0.03
	November 8	160	undetected	undetected	0.2	170	8	8	0.06
	November 9	1	undetected	undetected	0.14	2	undetected	undetected	0.07
	November 10	1	undetected	undetected	0.14	7	undetected	undetected	0.07
	November 11	1	undetected	undetected	0.16	5	undetected	undetected	0.09
Water works B	November 6	10	undetected	undetected	0.38	1	undetected	undetected	0.02
	November 7	7	undetected	undetected	0.27	3	undetected	undetected	0.03
	November 8	4	undetected	undetected	0.24	2	undetected	undetected	0.18
	November 9	3	undetected	undetected	0.22	5	undetected	undetected	0.09
	November 10	2	undetected	undetected	0.24	7	undetected	undetected	0.07
	November 11	2	undetected	undetected	0.19	3	undetected	undetected	0.04

and after using the toilet. The epidemic surveillance system was strengthened in key places such as schools, factories and nursing homes and a morning check and health inspection system was implemented. Diarrhea cases were persuaded to go to hospital for treatment. The hospital and family of patients implemented the following control measures guided by the CDC professionals: enteric isolation, cleaning of areas contaminated by vomit/excrement, suspension of the consumption of tap water, distribution of bottled/boiled water, cleaning and chlorination of the water cistern and stool sampling. The patriotic health campaign was carried out, and the garbage and feces of human and animals was removed in a timely fashion. From November 11 no new cases appeared, no epidemic occurred in schools or other crowed units and no severe hospitalization or deaths from gastroenteritis were recorded.

DISCUSSION

Norovirus exists mainly in contaminated water and is especially abundant in city sewage[6]. It is an important causative agent for human non-bacteria gastroenteritis, and the third most frequent pathogen for waterborne diseases[7]. In the guidelines for Norovirus outbreak issued by the Colorado Department of Public Health and Environment, if two positive results show in Norovirus tests of 2–6 patients' stool samples, then Norovirus can be considered the causative agent of the outbreak[8]. In the present study, we took eight stool samples and nine anal swabs from 17 symptomatic patients, meeting the China CDC's criteria of sample numbers for Norovirus[9].

Based on the clinical characteristics, epidemiological and environmental investigation findings, and laboratory test results, we concluded that this was an outbreak of gastroenteritis caused by waterborne Norovirus in tap-water from waterworks-A contaminated with sewage at source. The main supporting evidence is as follows: (1) The outbreak was characterized by a slow start followed by an explosive increase in the number of cases which could be linked to a common source; (2) Cases were highly localized in waterworks-A's supply area and relatively sporadic in waterworks-B's supply area; (3) The distribution of cases was highly consistent with the pipe network of waterworks-A; (4)Cohort study analyses showed that the RR of the AR in the residents who drank water from waterworks-A was 8.20 times of those who drank water from waterworks-B (RR=8.20, 95% CI:6.12–10.99); (5) The sanitation and quality control system of waterworks-A was not working well and the turbidity and free chlorine residual of pipe network water failed to meet the criteria for living and drinking water; (6) Norovirus with 100% homologous gene sequence was identified in fecal specimens from patients and sewage samples. These findings provided clear evidence of the causative agent and route of transmission.

The sanitary safety of drinking water has been of great concern in recent years[10-13]. There have been many cases of public health issues caused by consumption of drinking water. According to one surveillance report by the American CDC, among 28 waterborne disease outbreaks in 14 states during 2005–2006, 20 were related to drinking water[14]. Contamination of drinking water can cause gastroenteritis outbreaks. Periodic monitoring of indicator bacteria such as total coliforms and heat-resistant coliforms has been performed to identify drinking water contamination. However, surveillance data on viral pathogens in drinking water are scarce in China. The successful use of molecular methods to identify viral pathogens in the present study suggests that molecular techniques for drinking water surveillance could provide additional benefits for the quality control of drinking water and outbreak prevention.

In the present outbreak, the flow of River L, the water source of both waterworks A and B, was broken on October 26. Five days later, the cases of gastroenteritis in T1-T5 villages in the supply area of waterworks-A began increasing. The reason was found to be that the sewage outlet located 70 meters from waterworks-A contaminated the source due to backflow; the disinfection and purification of waterworks-A failed to meet health criteria; and Norovirus infected the residents through consumption of water from waterworks-A. Although River L resumed normal flow on November 4, the number of cases continued to increase and peaked at November 5 because waterworks-A did not correct the disinfection treatment. Control measures were undertaken on November 6 and case numbers began to decrease on November 8. The sanitary test results of waterworks reached the criteria on November 9 and there were no new cases from November 11. This outbreak indicates that waterworks should consider the location of sewage when choosing their water source, enhance the protection of the water source, and emphasize the quality control of disinfection treatment. When the quality of the water source decreases, disinfection treatments such as chlorine should be adjusted in time to ensure the safety of drinking water for residents. At the same time, surveillance should be continued.

Norovirus is characterized with acute illness, quick transmission and wide coverage[15]. Inadequate early measures or delayed control measures will probably cause an extended infection and make the outbreak curve trailing[16]. In our study, because the control measures commenced on November 6, five days after the increase in gastroenteritis cases was noticed, the curve dropped after one incubation period (2 days), and fell back to normal levels after two incubation periods (4 days). This shows that the measures were effective and timely. Throughout the course of the disease detection and control, there are two points worth noting. First, the improved disease surveillance system. The town hospital informed the local CDC when they noticed the abnormal increase of gastroenteritis cases to ensure early detection of the outbreak. Second, the effective emergency response mechanism. The department of health and CDC went to the field immediately after receiving the report from the hospital. Through investigation, the reason for the epidemic was found to be contamination of the drinking water supply. Multiple, targeted control measures were then initiated, including disinfection surveillance by the health department, water source protection by the water resources department, health education by the government and target population prevention by the CDC. All of these measures combined to bring the epidemic under control in a short time. It indicates that an effective disease surveillance system and emergency response mechanism are very important for the early warning and prompt control of similar outbreaks. The same conclusions were reached in a study of waterborne infectious disease reports over the last ten years in France: epidemiologic and environment investigation should be launched through established programs and continued for the length of the outbreak, and control measures such as public health surveillance depend on timely reporting and comprehensive lab tests[17].

Norovirus can be transmitted through multiple courses besides water, such as food, items and air[18]. Studies have documented that there are typically many infectors after a point-source outbreak of an epidemic, and these infectors can then be the source of infection again. The transmission can occur directly, through individuals or indirectly[19]. The main path of this outbreak is waterborne transmission, but other routes of transmission such as fecal–oral may also exist. This could explain why scattered cases occurred in the supply area of waterworks B while the majority of cases were located in the supply area of waterworks A. Because the clinical symptoms of Norovirus are usually mild and self-limited[20], some infectors may choose not to go to hospital, so the number of cases in this report probably underestimates the actual size of human infection. In addition, while November is the peak season for local autumn diarrhea[21], the cases among the age group 1–5 years was significantly higher than that of other age groups. It is necessary to investigate further to determine if all the cases in this young age group were infected by contaminated water. Moreover, some cases of diarrhea in the community did not visit the doctor and therefore could not be analyzed in our study. This deficiency in reporting needs improvement in the future to ensure rapid and targeted response to outbreaks of gastrointestinal illness.

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