Research Paper

Norovirus Gastroenteritis Outbreak in Kurdistan Province, Iran: Contamination of the Water Supply System

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ABSTRACT

Background: Noroviruses are the most common known causes of non-bacterial acute gastroenteritis worldwide. Norovirus gastroenteritis usually presents with vomiting and diarrhea in the winter.

Methods: This cross-sectional study was conducted to evaluate the outbreak of gastroenteritis in one of the villages of Kurdistan Province, Iran, from February 1 to 12, 2019. In this period, 149 people developed joint illness and symptoms of diarrhea, vomiting, and abdominal cramps, whose information was recorded. Data analysis was done with Stata7 software.

Results: The attack rate of the total population in the village was 31.17% (26.5% in men and 36.24% in women). The median age of the patients was 26.5 years. The mean patients' age on the first days of the outbreak was less than on the other days, and this relationship was statistically significant (P=0.003). The most common symptoms were non-bloody diarrhea (57.71%), vomiting (52.34%), abdominal cramps (26.17%), and nausea (24.83%). According to the shape of the epidemic curve, the outbreak was a community-wide outbreak caused by the norovirus.

Conclusion: Based on clinical evidence, epidemiological examination, and human and water samples analyses, outbreaks occurred due to the consumption of drinking water contaminated with norovirus. To prevent similar outbreaks, it is recommended to fix the bugs observed in the water supply system and implement the water safety program.

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1. Introduction

Outbreaks of water and foodborne illnesses contaminated with pathogenic microorganisms are a major public health problem in the world [1]. The World Health Organization defines outbreaks of water and foodborne illnesses as follows: if two or more people have the same digestive symptoms and have used a common food or drink at the same place [2]. The cause of most foodborne illnesses are bacteria, bacterial toxins, parasites, and viruses [3].

Acute gastroenteritis due to gastrointestinal infection presents with abdominal cramps, nausea and vomiting, diarrhea, and in some cases, fever and headache. Noroviruses and rotaviruses account for most cases of acute gastroenteritis. Norovirus is the most common cause of gastroenteritis in adults [4, 5]. According to Bányai et al., noroviruses affect people of all ages and are a leading cause of foodborne diseases and outbreaks of gastroenteritis worldwide [6]. Noroviruses are more common in hospitals, nursing homes, schools, and kindergartens [7]. The virus's incubation period is 10 to 51 hours, and the disease is generally self-limiting and usually lasts 2-3 days [8, 9]; however, the duration of illness in children under 11 years may be 4 to 6 days [10].

The World Health Organization [2] estimates that noroviruses cause 685 million cases of diarrhea and 212489 deaths annually [11]. In Iran, noroviruses are one of the causes of diarrhea. Romani et al. in the study of noroviruses infections in people over the age of 18, concluded that noroviruses are the causes of diarrhea in hospital emergencies [12].

Primary cases are often due to exposure to contaminated food or water, while person-to-person contact may further spread infection. Infected people dispose of many viral particles into the environment, and shedding (low level) may continue after symptoms are resolved [9, 13].

Noroviruses are highly infectious and transmissible, as only 10 virus particles can cause infection and affect people of all age groups. It often occurs in the winter with vomiting and diarrhea [14, 15]. Humans are the only known reservoir for noroviruses. The virus is transmitted in three ways: person to person, contaminated food, and water. Person-to-person transmission may occur through the stool and oral route [16, 17]. In recent years, the dominant genotype worldwide has been genotype II type 4 (GII.4), but new genotypes appear every 2-4 years [18].

Noroviruses cause more than 14000 hospitalized patients, 281000 emergency patients, and 627000 outpatient visits of children under 5 years old at US children's hospitals. Norovirus is responsible for the deaths of 70000-200000 elderly people worldwide [6].

Measures to control norovirus outbreaks are limited, mainly involving health interventions and case isolation. Therefore, disseminating knowledge about norovirus infection among staff is critical to controlling the spread of the disease during outbreaks [19].

We designed this study to describe the overall pattern of the outbreak and identify the possible causes (factors) that have contributed to its formation. This study was performed to investigate the outbreak of norovirus gastroenteritis in a village in Kurdistan Province in 2019. With informed reviews to identify the factors and ways to control and prevent these outbreaks, health care costs can be saved, and community health is improved.

2. Materials and Methods

The study was a cross-sectional descriptive-analytical one. It was performed on patients with gastroenteritis in one of the villages of Kurdistan Province, Iran, from February 1 to 12, 2019. During this period, 149 people developed joint illness and symptoms of diarrhea, vomiting, and abdominal cramps, whose information was recorded (Table 1). We only included cases living in the village a week before the outbreak, whether permanent or temporary. However, we excluded cases with incomplete information. The data were entered into the SPSS software v. 16 and analyzed by descriptive statistics and statistical tests. The statistical significance level was considered 0.05.

Outbreak description

The first step in investigating an outbreak is to confirm it by diagnosing the reported cases. In gastroenteritis outbreaks, the syndrome diagnosis is most often made in the early stages. Then, the etiological diagnosis of the disease is made. Upper Zagheh Village is located in the Divandareh area in Kurdistan Province, Iran. The village is 35 km distance from Divandareh City.

On February 1, the Emergency Department of Imam Khomeini Hospital reported several patients in the Upper Zagheh Village with similar symptoms of nausea, vomiting, and abdominal pain.

At 9:20 PM, the outbreak team went to the hospital. It is known that 15 people with common gastrointestinal symptoms have come from the village. So the city's rapid outbreak assessment team arrived at the village at 11:20 PM. After reviewing the situation, the outbreak was confirmed. After the outbreak was confirmed, outbreak teams warned, and the outbreak control program, treatment of patients, and epidemiological and environmental studies were reviewed.

Sources of disease detection and diagnosis

One nurse was appointed in the hospital to report the identified cases to the Health Center and was selected to identify and detect disease in the hospital during office hours. The appointed nurse reported cases of illness from all parts of the hospital (especially in the hospital emergency) daily. During non-office hours, the supervisor was responsible for investigating and reporting identified cases each evening. Other reporting sources included the village's comprehensive health services center and public and private medical diagnostic laboratories that report cases daily, both morning and evening.

Laboratory information

A total of 42 human rectal swab specimens were examined in vitro. The collected samples were sent to the Health Center Laboratory for testing. The specimens were evaluated for parasitic factors and serological tests of HEV IgM and HAV IgM. The samples were sent to the Health Reference Laboratory and examined for *E.coli* infection.

Environmental assessment

Experts assessing the area's rapid environmental footprint observed that the sewage of 25 households on the eastern side of the village enters the environment and agricultural land and then the village river without any purification. The upstream of this water source is the farmland, where the villagers add their animal waste for greater productivity. Also, two days ago, a villager redirected the sewage flow of 25 households to the village's water provider sources and springs. This event increases water turbidity. Also, the residual chlorine in the water was zero.

Water supply system status

The water provider sources were located south and north of the village, respectively. A well (18 m depth), one spring in the south of the village, and one water storage source were located in the northern part of the village. The well and water source were located downstream of the village, and their distance to the upstream reserve is approximately 2 km. The water provider well was located within the village river and very close to the surface water within the river.

Chlorination system status

Chlorination of the village water was done semi-manually and had no hypochlorinator. The chlorination method of the village drinking water was that the chlorine powder was mixed in a 100-L barrel with water and flowed into the supply source through the valve.

Contaminant sources

Two possible sources of contamination of the village's potable water were a deep well and a spring. The well was located at the side of the river, so the sewage of 25 households in the village was discharged into it (a source of water pollution). The water fountain is 100 m away from the well, which is contaminated by the sewage of 25 households and farmland using animal manure.

3. Results and Discussion

The demographic and epidemiological features of the outbreak was shown in Table 1. The highest incidence rates of disease were observed in people 11-15 years old (85%), then 16-20 years (50%), and finally children under 5 years (48.93%) (Table 2).

The Mean±SD age of the patients was 28.54±19.84 years (the infection age range: 1-75 years). The Mean±SD age in male patients was 28.36±19.57 years, and in female ones, 28.68±20.18 years, which were not statistically significant (P=0.922). The mean age of the patients on the first to third days of the outbreak was lower than that on the other days, and this relationship was statistically significant (P=0.003).

According to the results, 44.3% (n=66) of the patients were male and 55.7% (n=83) female. About 37.6% (n=56) of the people involved in the outbreak were homemakers, and 22.8% (n=34) were farmers and ranchers. Of the total cases, 12.8% (n=19) were hospitalized (inpatient), and the rest were treated as an outpatient. Re-admission rate was 4.7% (n=7). Re-admission was due to failure to resolve symptoms after initial treatment or re-infection (Table 3).

The outbreak had two incremental peak cases. This outbreak was a double peak occurrence of cases. Most

Table 1. Demographic and epidemiological features of the outbreak in Kurdistan Province, Iran

Row	Demographic and Epidemiological Features	No.(%)
1	The total population of the village	478 people
2	Total households involved in the outbreak	52 household
3	Total households with wells	57 households
4	Households without wells	20 households
5	Households with wells and diseases	37 households
6	The incidence rate of the outbreak in the total rural population	31.17
7	The incidence rate of women in rural areas	26.50
8	The incidence rate in men in rural areas	36.24

cases occurred on the fourth day of the outbreak (incidence rate is 9.63 per 100000) (Figure 1).

The most common symptoms were non-bloody diarrhea (57.71%), vomiting (52.34%), abdominal cramps (26.17%), and nausea (24.83%). The least common symptoms were anorexia (3.35%), lethargy (3.35%), and fever (9%) (Table 4). According to the shape of the epidemic curve, the outbreak was a community-wide outbreak caused by the norovirus virus. The drugs prescribed for patients were ciprofloxacin (n=45), azithromycin (n=27), cefixime (n=21), and metronidazole (n=27).

Environmental survey results

Chlorine measurement

From March 21, 2018, to February 11, 2019, 158 chlorine measurements were carried out in the village's water distribution system, resulting in 91% favorable, 3% below range, and 6% zero. On the day of the outbreak, 6 water chlorine measurements were performed, all of which were declared zero. Also, in the water tanker chlorine measurement, 86% was favorable, 11% zero, 3% lower than the range, and no result was higher than the range. The chlorine of drinking water was measured using a chlorination kit. The data showed that the disease occurred along with a decrease in water chlorine

Microbial sampling

On February 1 (outbreak day), three microbial samples were taken, all of which were inoculated. Microbial tests from samples taken from the drinking water distribution network, raw water supply sources, well water supplies, and the village water storage sources included a thermoplastic coliform test.

In 2019, except in April, October, and December, a microbial sampling was carried out every month from the water distribution network of the village, and all samples were drinkable (9 times in total). From January 21 to February 9, 18 water samples were taken from the distribution network. Fifteen cases were drinkable, and 3 cases were non-drinkable. Also, during the flood, 22 microbial samples from rural private wells, 3 microbial samples from spring water, and 4 microbial samples from mobile tanker water were performed. All samples were drinkable. The drugs prescribed to patients were ciprofloxacin (n=45), azithromycin (n=27), cefixime (n=21), and metronidazole (n=27) (Figure 2).

Noroviruses are among the most important causes of acute non-bacterial gastroenteritis both at health care centers and at other society organizations. Although the mortality from norovirus gastroenteritis is typically limited to children and the elderly, this disease has significant consequences and has an economic-financial burden on the health care system [20].

Because of the genetic diversity of the virus and the ongoing viral evolution, currently, the only method of combating the virus is taking infection control and prevention actions. Little research has been done on the vaccine and treatment of this disease in humans. However, recent discoveries and studies in mice have shown that specific biological factors can slow or kill the virus [21].

Owning to the ways of transmitting the disease, and implementing standard precautions in the care system reduces transmission [22]. One of the main control strategies recommended for stopping the transmission of noroviruses during outbreaks is proper hand hygiene [23]. Handwashing with soap and water is recommended

Table 2. Gastroenteritis disease incidence by age group in Kurdistan Province, Iran

Age (Y)	Incidence Rate/No.(%)
>5	23(48.93)
5-10	10(20.84)
11-15	17(85)
16-20	12(50)
21-25	10(32.25)
26-30	17(34.7)
31-35	4(8.51)
36-40	14(30.43)
41-45	12(41.37)
46-50	8(25.80)
51-55	6(27.28)
56-60	0(0)
61-65	12(44.45)
<65	4(10)
Total	149(31.17)

Table 3. Frequency distribution according to the variables studied

Variables		No.(%)
Gender	Male	88(44.3)
	Female	83(55.7)
Occupation	Farmer–Rancher	34(22.8)
	Student	29(19.5)
	Housewife	56(37.6)
	Child	27(18.1)
	Free	3(2)
Type of treatment	Inpatient	19(12.8)
	Outpatient	130(87.2)
Revisit	Yes	7(4.7)
	No	142(95.3)

Table 4. Distribution of disease cases by clinical signs and symptoms

Symptoms	No.(%)
Non-bloody diarrhea	86(57.71)
Bloody diarrhea	11(7.38)
Vomit	78(52.34)
Nausea	37(24.83)
Abdominal cramp	39(26.17)
Fever	9(6.04)
Anorexia	5(3.35)
Lethargy	5(3.35)

for at least 20 seconds after the patient's contact with confirmed or suspected cases [24]. For this reason, health experts have taken standard precautions during the outbreak and in dealing with patients and the outbreak site.

In microbial laboratories, standard precautions are also necessary. A study was conducted in Germany to investigate the inhibitory effect of three types of alcohol (ethanol, 1-propanol, and 2-propanol) on norovirus in vitro and in vivo. The study results showed that ethanol and 1-propanol have a higher viral load capacity than 2-propanol [25]. In this outbreak, we provided laboratory personnel with training on disinfecting samples, hands, and surfaces after performing laboratory tests.

Investigating and reporting outbreaks of disease is particularly important in caring for communicable diseases. Lessons learned from a review of the outbreak were used for formulating health policies, preventing absenteeism, reducing financial costs (for the individual and the health system), impacting the outbreak on society, and recording virus outbreak control experiences. In the Hong Kong health system, they reduce the prevalence of norovirus transmission in their seven hospitals [26], using the experiences of controlling other outbursts.

During this outbreak, many rural people from all age groups were affected, and this volume of infection in various age and sex groups indicated the potential for norovirus transmission. From 2014 to 2017, about 692 outbreaks of non-bacterial gastroenteritis were reported in Europe, 89% were due to norovirus. This finding is consistent with the prevalence data of many developed countries. In all of these outbreaks, the virus was highly

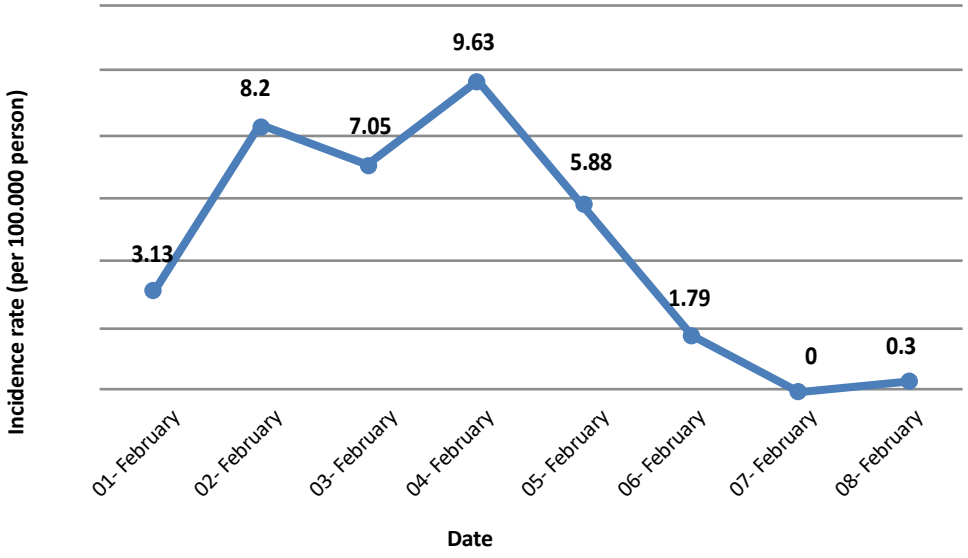

Figure 1. Outbreak curve by incidence rate

*Feb: February.

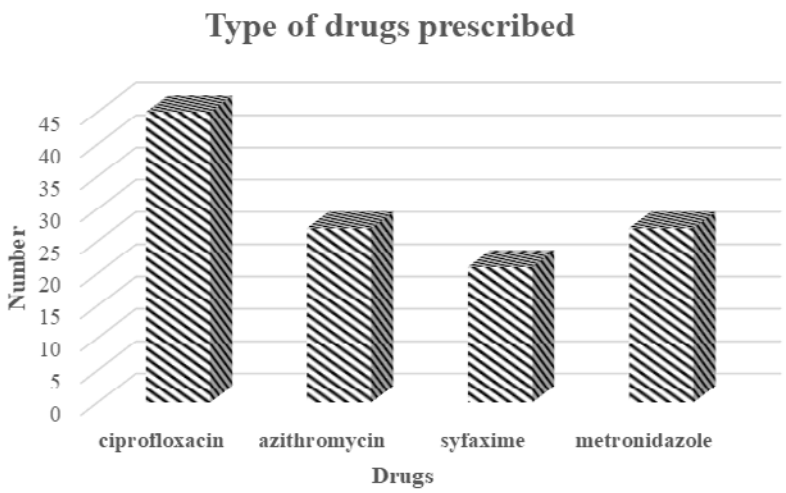

Figure 2. Drugs prescribed for the patients understudy

transmitted [11]. Similarly, in the United States, noroviruses account for almost two-thirds of all non-bacterial gastroenteritis cases [15].

Norovirus is highly contagious and spreads rapidly in crowded and closed areas such as kindergartens, nursing homes, schools, and other places where people have close contact, most often through person-to-person transmission [27]. There was also a person-to-person transmission of norovirus in this outbreak. The Mean±SD of the transmission interval was 2±1 day. This finding is consistent with previous studies in the United States and other countries [8, 27].

Low doses are needed to cause infection and environmental viability of norovirus and increase secondary transmission through contaminated fluid, hands, and other forms of contact. One study showed that students who cleared the vomiting of other students with norovirus gastroenteritis became ill after an incubation period due to secondary infection [15]. In several studies, water contamination with norovirus despite wastewater treatment has been demonstrated, and the viral concentration burden is higher in the colder months [28].

The disease is associated with age groups and is more common in young children and people older than 65. In Grytdal et al. [29], the highest incidence among inpatients were in older adults (38 per 100000 in 65-84 years old and 70 per 100000 in 70 years and older). However, in outpatients, the highest norovirus incidence was in 45 to 64 years (368 per 100000) and lower rates in ≥85 years (198 in 100000). This finding could be due to the small sample of patients admitted to the high age group 29. In our study, the highest incidence of disease was in the age group of 11-15 years (85%), 16-20 years (50%), and children under 5 years (48.93%). Of outpatients, 13.34% were over 60 years which was consistent with the study results by Qi et al. [30].

Most of the outbreaks occurred in the fourth quarter (40.8%) and the first quarter of the year (34.7%), consistent with our study. The incidence of viral gastroenteritis in temperate climates often occurs during the cold months of the year. With the onset of autumn, there is a possibility of widespread norovirus gastroenteritis epidemics. Low-temperature conditions can cause the virus to persist, explaining the greater prevalence in the cold season [31]. This finding is consistent with a study by Lian et al. [32].

However, norovirus gastroenteritis is a self-limiting disease with a short duration of illness that most patients, especially adults, recover without specific treatment and ultimately require no hospitalization. However, in our study, 8 patients needed hospitalization, which was indicative of the severity of the symptoms [21]. These results are consistent with some previous studies [33, 34].

Symptoms of viral gastroenteritis are more severe in children younger than 2 years and pregnant women. Norovirus infection in term and preterm infants causes a wide range of symptoms but may be associated with severe complications such as enterocolitis necrosis [35]. A retrospective study showed that 1 out of 8 neonates with viral gastroenteritis develops necrotizing enterocolitis [36].

Infants and the elderly with clinical symptoms are at increased risk for complications due to weaker immune systems. No cure for the disease has yet been proven. However, a double-blind clinical trial showed that nitazoxanide use in children was associated with a reduced duration of illness [37].

In our study, the most common symptoms were non-bloody diarrhea (57.71%) and vomiting (52.34%). However, in the study of Hatami et al., the most prominent symptoms were vomiting (94.9%), diarrhea (37.7%), abdominal pain (18.8%), and fever (0.6%) [38].

Based on clinical evidence, epidemiological examination, and results of human and water samples analysis, the disease outbreak in this study was due to the consumption of drinking water contaminated with norovirus. Water pollution has been caused by the entry of domestic wastewater into the water supply system. Secondary transitions have occurred after these factors affected many people in the village. So far, limited studies in Iran have investigated the outbreak of gastroenteritis caused by noroviruses. Our study could help investigate and report norovirus gastroenteritis outbreaks.

4. Conclusion

To prevent similar outbreaks, it is recommended to fix the bugs observed in the water supply system and implement a water safety program. Also, it is recommended to provide equipment for identifying norovirus and other water-borne microorganisms in water reference laboratories and provide staff with practical training in the relevant tests. It is expected that the information in this study may have helped reduce the prevalence of outbreaks of water and foodborne illnesses and to improve the methods of controlling outbreaks of norovirus gastroenteritis.

Ethical Considerations

Compliance with ethical guidelines

All procedures followed the ethical standards of the responsible committee on human experimentation (institutional and national) and the 1975 Declaration of Helsinki.

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Authors' contributions

Methodology, investigation, formal analysis, writing, and project administration: Seyede Parvin Ghazaei; Methodology, investigation, Scientific advisor: Meysam Olfatifar; Methodology, investigation, formal analysis, and writing the original draft: Ardashir Rahimzadeh; Mansour Mirzaei and Hadi Rezaei and Mansour Navshad and Payam Shokri and Khosro Kazempour: Writing - review, editing, and project administration.

Conflict of interest

The authors declared no conflict of interest.

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