

Epidemiological characteristics of viral gastro-enterocolitis outbreaks in Sofia province, Bulgaria, during the period 2007 – 2022

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Abstract

The aim of the first study of viral gastroenterocolitis epidemic outbreaks during a 15-year period in a region of Bulgaria, with the elucidation of epidemiological characteristics in terms of etiological structure, clinical diversity and severity, intensity, dynamics, as well as an outline of their significance in the context of the modern level of medical development and current organization of healthcare in this country. The subject of the epidemiological survey was Sofia Province, which has specific geographic, economic, ethnic and social characteristics as neighboring with the capital. The epidemiological study considers thirteen viral gastroenterocolitis epidemic outbreaks during the period under review, characterized by intensity, range, etiology and clinical diversity. Between 2007 and 2022, 4 municipalities in the region with compact Roma population were affected - Samokov, Ihtiman, Pravets and Elin Pelin, as well as a university hospital in Sofia, providing services also to the population in the region.

Keywords: Norovirus; Rotavirus; Gastroenterocolitis; Epidemic; Outbreak

1. Introduction

Norovirus infection is a gastrointestinal human disease caused by viruses of the family Caliciviridae, genus Norovirus. Human noroviruses known to date belong to three genogroups (GI, GII, and GIV) including more than 30 genotypes. New norovirus strains appear once every 3-4 years. Most prevalent are noroviruses of genogroup II, genotype 4. Noroviruses cause approx. 18% of all acute gastroenteritis cases worldwide [1]. Most often, during outbreaks, primary cases emerge after contaminated food/water consumption, while secondary and tertiary cases are due to direct human-to-human transmission [2]. This feature of epidemic outbreaks caused by noroviruses is instrumental in their distinction from bacterial outbreaks [3]. The aim of the present study was elucidation of epidemiological characteristics of viral gastroenterocolitis epidemic outbreaks registered during the period 2007 – 2022 in Sofia Province.

2. Material and methods

Epidemiological information from the Regional Health Inspectorate – Sofia Province concerning gastroenterocolitis epidemic outbreaks was considered through epidemiological observations, analysis and forecasting.

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3. Results and discussion

The first registered viral gastroenterocolitis outbreak in Sofia Province during the period 2007 – 2022 was reported in the town of Samokov. Between 06 – 25.02.2007, 977 cases with gastrointestinal complaints were registered there. The actual number of cases was probably several times greater. Infections were registered in all districts of the town. The daily chart of emerging cases is shown in Fig. 1.

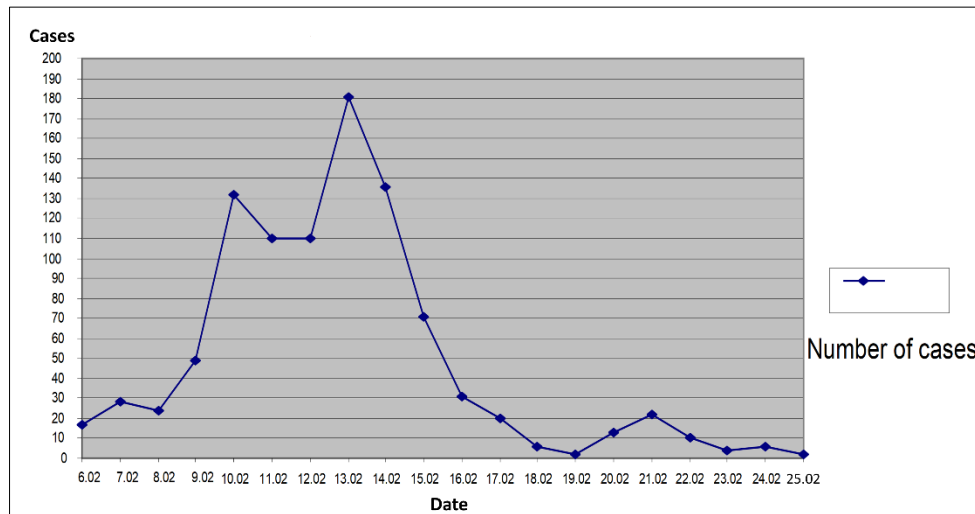


Figure 1 Daily chart of emerging cases with gastrointestinal complaints in the town of Samokov during the period 06 – 25.02.2007

The town water supply is centralized and its investigation did not find indications of failures in the pipe network. Water was being disinfected with reliable methods. Performed chemical and microbiological investigations did not show deviations from adopted state standards.

Age distribution of cases was the following: 0 to 3 yr – 186 cases, 4 to 7 yr – 158 cases, 8 to 19 yr – 186 cases, 20 to 60 yr – 352 cases and above 60 yr – 95 cases.

Clinical characteristics of observed patients displayed a uniform course of disease. The first symptoms were nausea, persistent vomiting and abdominal pain, with or without diarrhea, while most often these symptoms were combined. Less often, myalgias, malaise and headache were observed. The majority of patients were afebrile, while a smaller fraction of them had subfebrile temperature. Their diarrheal stools were not abundant, ranging from mushy to watery, without pathological admixtures, with frequency between 4 and 6 defecations per 24 hours. Disease progression was mild in most cases.

Microbiological testing of fecal samples from patients did not reveal an etiological agent.

Virological tests of fecal samples from 36 children were performed for rotaviruses with “Ridascreen Rotavirus” EIA, for enteroviruses – with isolation of cell cultures and for noroviruses – with RT-PCR. Results were negative for rota- and enteroviruses, but in 11 samples (31%) norovirus RNA was evidenced. In addition, 90 fecal samples from children up to 10 yr of age were tested with two diagnostic methods: „Ridascreen Norovirus“ EIA and RT-PCR. Eleven of them (12%) were positive for NV-Ag and 7 (8%) revealed norovirus RNA [4].

This was the first norovirus epidemic outbreak registered in Sofia Province that progressed with highest intensity of infection [5].

In the same year, during the period 01.07. – 14.08., this time in the town of Ihtiman, 43 enterocolitis cases were registered. They were from several districts of the town with compact Roma population. Most affected were children of up to 2 yr of age. The age distribution of cases was the following: 0 to 1 yr – 19 children; 1 to 2 yr – 13 children; above 2 yr – 11 children.

Performed microbiological and virological tests are presented in Fig. 2.

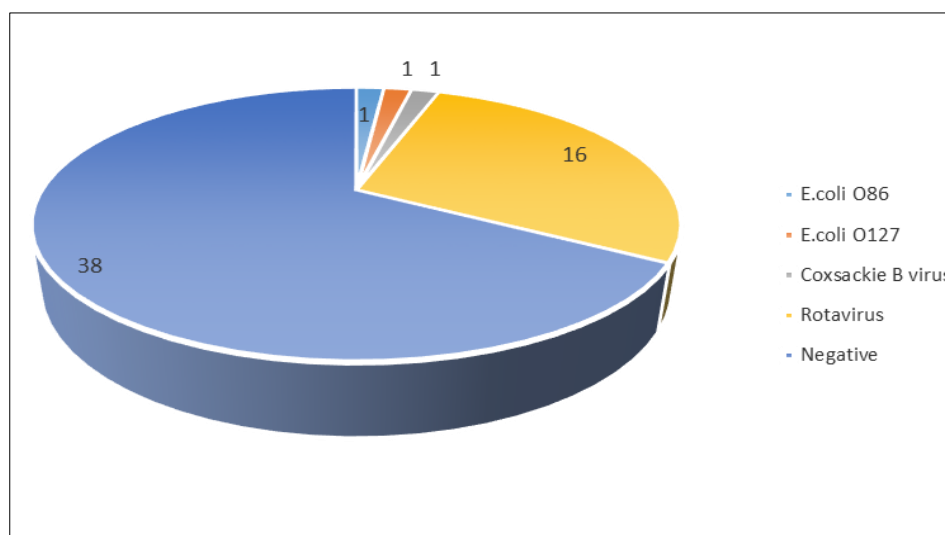


Figure 2 Distribution of revealed causative agents during the period 01.07. – 14.08.2007 by performed virological tests of the gastroenterocolitis epidemic outbreak in the town of Ihtiman

Following the chronology, we present studies of 4 nosocomial outbreaks of intestinal infections during different periods within 2008 in St. Anna University Multiprofile Hospital for Active Treatment which is one of the biggest university hospitals in the capital that provides region-related services also to citizens of Sofia Province.

The first nosocomial outbreak was registered in January, emerging in the 2-nd Internal Medicine Unit of in St. Anna University Multiprofile Hospital for Active Treatment, Sofia during which 10 patients were infected within 1 week. Clinical progression of the disease was characterized by sudden appearance of a diarrheal syndrome /multiple watery defecations without pathological admixtures/. In some cases, clinical progression was with abdominal pains, nausea, vomiting and body temperature rise /up to 38°C/. No patient was diagnosed with catarrhal phenomena of the upper respiratory tract. After symptomatic and antipathogenic treatment, patients' general condition improved in 1-2 days. Consumption of one and the same food product by patients was not detected. The hospital unit was found to maintain a satisfactory sanitary-hygienic and anti-epidemic regime. No hygiene mishaps were found also during inspection of the hospital kitchen. Performed microbiological tests did not reveal a pathological agent. Fecal samples were tested in the National Reference Laboratory for Enteroviruses at the National Center of Infectious and Parasitic Diseases. With RT-PCR, 5 of the 10 samples showed norovirus positive.

The second nosocomial outbreak in the same unit was registered in the middle of February 2008 and lasted for 40 days. Twenty-five persons were infected, including 6 persons from the staff. Clinical progression did not differ from the previous outbreak in January. Out of 15 fecal samples tested in the National Reference Laboratory for Enteroviruses at the National Center of Infectious and Parasitic Diseases, 7 samples revealed norovirus RNA or antigens. Anti-epidemic measures were taken for limiting the outbreak, including stop on admissions.

The third nosocomial outbreak was registered in the middle of April 2008, again in the same unit, and lasted for 1 week. Seven persons were infected. Their microbiological tests did not show positive results. Four of the patients underwent virological testing whereby norovirus RNA or antigens were revealed in 2 of them.

The fourth nosocomial outbreak was reported in the end of November and the beginning of December 2008. It was distinctive with simultaneous outset in both internal medicine units of the hospital. Twenty-six patients were infected, of which 6 in the 1-st and 20 in the 2-nd Internal Medicine Unit. Eighteen of the patients underwent virological testing, whereby norovirus RNA or antigens were revealed in 8 of them: 5 in the 1-st and 3 in the 2-nd Internal Medicine Unit.

Necessary anti-epidemic and sanitary-hygienic measures were taken for limiting the spread of infection during the for nosocomial outbreaks. All patients with close to severe clinical progression of infection were taken to intensive care units. Orders were issued for prohibition of visits with patients and access of unauthorized persons to the affected units, for strict observation by medical staff of the rules for efficient hand disinfection during provision of services for patients

as well as to intensify disinfection routines. In order to interrupt the transmission mechanism, it was recommended to the management of the affected units to provide services for infected patients with separate staff.

During the 4 outbreaks of nosocomial infections, 68 persons were infected. All of them were tested for presence of bacterial pathogen. Virological testing with RT-PCR was performed in 47 cases, 42 of which were patients and 5 contact persons. The results revealed noroviruses in 22 fecal samples, 20 of which from patients, 1 from a nurse who developed gastroenteritis symptoms and 1 from a contact person [6].

A conducted epidemiological study did not find violations of anti-epidemic regime and sanitary-hygienic routine in the affected hospital units. There were no staff members there, as well as in the rest of the hospital units, with intestinal infection symptoms, no hygienic mishaps were found in the hospital kitchen, also with staff testing. All the above points to the possibility that visitors were the source of these nosocomial outbreaks in the units with mild or asymptomatic progression of infection.

It is known that about 30% of norovirus infections progress without clinical features but are accompanied with viral shedding in high concentrations (10^6 - 10^8 virus particles/gram of feces) [6]. Probably, infection had spread through human-to-human transmission or contaminated objects in patients' surroundings [6].

In the same year, during the period 13.07. – 29.09., an enterocolitis epidemic outbreak was registered in the town of Ihtiman where 56 persons were infected. Seven cases were from the town itself and all the rest – from the “New” and the “Old” neighborhoods with prevailing Roma population.

The age distribution of cases was the following: up to 1 yr – 2 children, from 1 to 2 yr – 26 children, from 3 to 5 yr – 11 children, from 20 to 60 yr – 5 adults and above 60 yr – 2 adults.

Disease progression was mild to moderate with body temperature rise up to 39°C, generalized weakness, vomiting and repeated diarrheal defecations, mixed with mucus and blood in few cases. The symptoms subsided in 3-4 days.

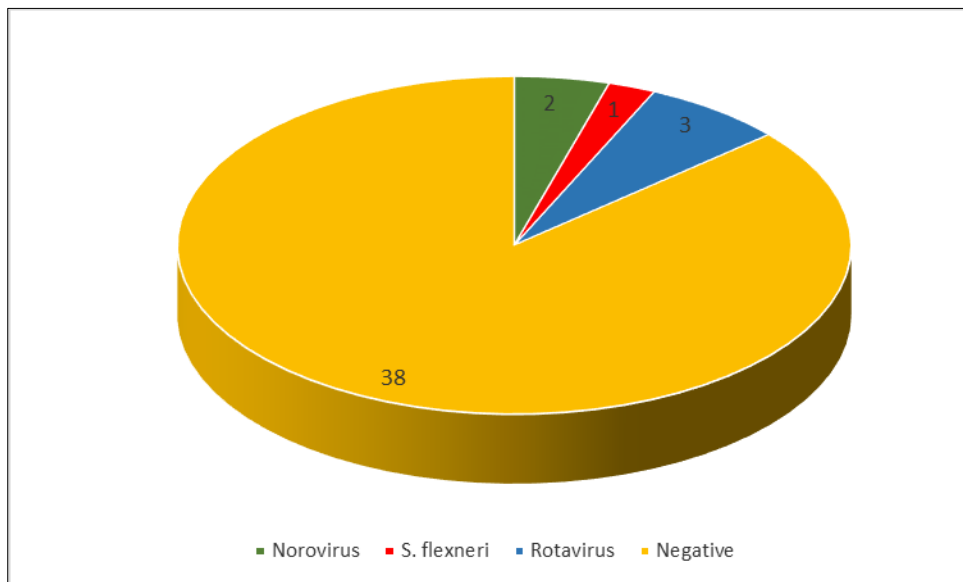


Figure 3 Distribution of revealed causative agents during the period 13.07. – 20.09.2008 by performed virological tests of the gastroenterocolitis epidemic outbreak in the town of Ihtiman

A conducted epidemiological study found that microbiological and chemical monitoring of tap water was carried out regularly and according to water safety regulations. No deviations were found in its characteristics.

During the period 12.10. - 25.10.2010, in the village of Stolnik, Elin Pelin municipality, a rising number of enterocolitis cases was observed, with 17 persons sought medical care. A conducted epidemiological study found that:

- During these two weeks, intestinal infections morbidity in the population was significantly higher, without active seeking for medical care due to mild disease progression;
- The diseases were characterized by mild to moderate progression, most frequently starting with multiple vomits accompanied by subfebrility, followed by watery defecations, without mucus and blood admixtures. Symptoms in mild cases subsided in 1-2 days while those in severe ones subsided in 3-4 days.

In the outbreak zones, almost all cases appeared within an interval of 2-3 days. In a study conducted at patients' homes, fecal samples were taken for microbiological testing of patients and contact persons, all with negative results. The age distribution of cases was the following: up to 1 yr – 0 children, from 1 to 4 yr – 3 children, from 5 to 16 yr – 5 children, from 19 to 35 yr – 6 adults, above 35 yr – 3 adults.

The epidemiological study found deviations in the quality of village tap water (turbidity).

Pipe network water from different locations in the village of Stolnik and from the local sources was analyzed. The first samples from the village and the local water source in the vicinity of Eleshnitsa village showed unsatisfactory results. According to the CDC and WHO clinical and epidemiological criteria for norovirus gastroenteritis epidemic outbreaks (Kaplan et al., 1982), i.e. negative results for bacterial pathogens and parasites, vomiting in >50% of cases, 24-48 h average incubation period, 12-68 h mean disease duration, the epidemic outbreak in the village of Stolnik was defined as one of norovirus etiology.

Two years later, during the period 26.03.–02.04.2012, at the Regional Health Inspectorate of Sofia Province in the town of Samokov, evidence was received about significant rise in the number of acute gastroenteritis cases. To that date, the number of registered cases had reached 661.

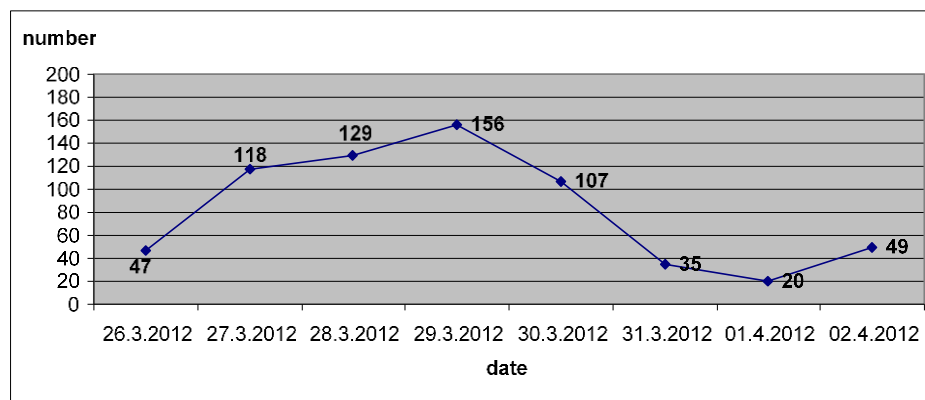


Figure 4 Daily chart of the number of viral gastroenteritis cases in the town of Samokov during the period 26.03.-02.04.2012

By 16.04.2012, the number of cases in the town and its municipality had reached 754. They were registered in all districts of the town as well as several neighboring populated places.

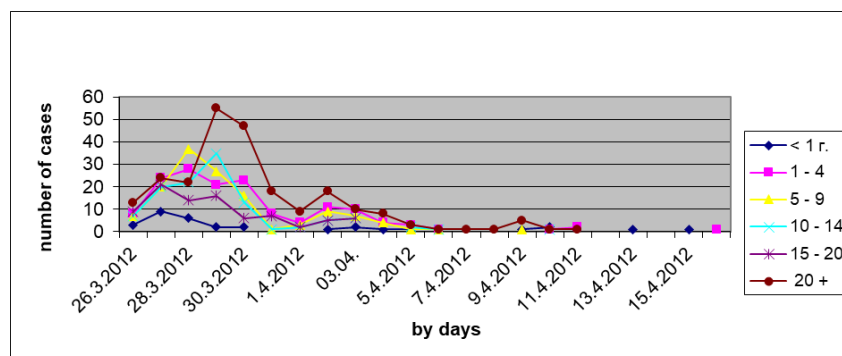


Figure 5 Age distribution of viral gastroenteritis cases and their registration dates in the town of Samokov during the period 26.03.–16.04.2012

The age distribution of cases and their registration dates are presented in Fig. 5.

The majority of patient complaints appeared on 26.03. and the early hours of 27.03.2012. The diseases had mild to moderate progression, while being clinically characterized by multiple vomits combined with heaviness and nausea, seldom with abdominal pains and febrility. After approx. 4 to 6 hours, some of them also had diarrheal watery defecations without pathological admixtures. No catarrhal phenomena of the upper respiratory tract were observed. Paraclinical tests did not reveal significant deviations. The mean disease duration was between 12 and 60 h combined with dehydration, particularly in young children. After rehydration, symptomatic and antipathogenic treatment, patients' general condition improved in 2-3 days.

Parasitological examination performed by the Regional Health Inspectorate – Sofia Province showed negative results for blastocysts and lamblia. Microbiological examination at St. Anna University Multiprofile Hospital for Active Treatment did not reveal pathogenic intestinal bacteria.

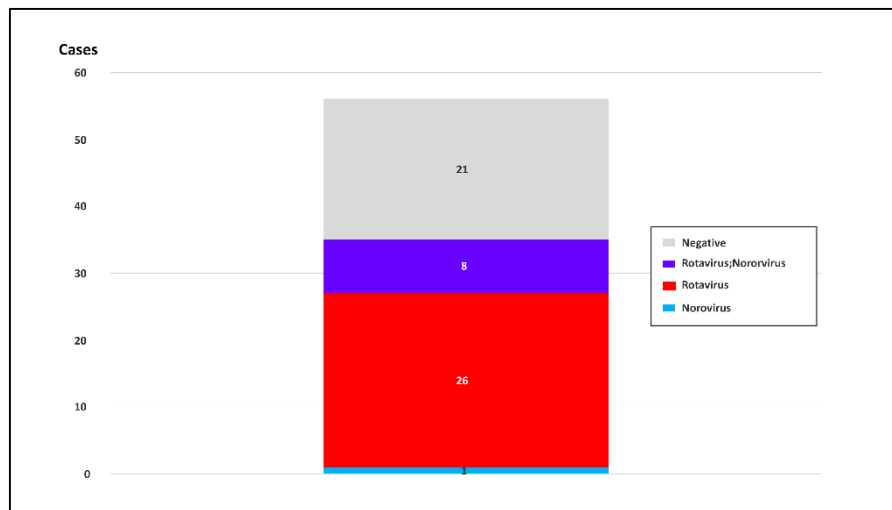


Figure 6 Distribution of revealed causative agents during the period 26.03. – 16.04.2012 by performed virological tests of hospitalized patients at the time of the gastroenteritis epidemic outbreak in the town of Samokov

Before the outbreak, there was no evidence of pipe network failures. The town of Samokov is supplied with water from the Beli Iskar Dam. Initially, we thought that a point source of pollution existed and, having in mind the high infection rate in the town, it was likely that tap water was contaminated. Intactness of the pipe network and the negative results of tested water samples rejected the hypothesis of fecal contamination. Patients' medical history did not reveal any common source of food poisoning. Disease progression, even distribution of cases over the town territory as well as frequent cases of family cluster infections defined social contact-based transmission as the most probable in this epidemic outbreak.

A year later, again in the Samokov region, a gastroenterocilitis epidemic outbreak was registered. During the period 01.08 - 30.11.2013, altogether 100 cases were registered, 68 of which in the Roma population. The age group up to 1 yr (35 cases) was most affected, followed by the 1-4 yr (28 cases). In all other age groups, single cases were registered. The sex distribution of patients was 47 males and 53 females. In the course of the epidemic, 7 outbreaks, with 2 cases each and 86 outbreaks, with 1 case each were registered.

Clinical progression of the disease lasted from 1 to 4 days, with emergence of body temperature above 38° C, malaise, nausea, multiple vomits, epigastric pain and 1-2 diarrheal defecations [7].

The conducted epidemiological survey did not reveal failures in the pipe network. Such evidence was reported by the inhabitants of the Roma neighborhood where the outbreak started and 75% of the gastroenteritis patients were registered [7]. Performed chemical and microbiological investigations of tap water did not reveal deviations from adopted state standards. No food product was detected, which had been consumed by the patients, posing a potential safety hazard. These data and the frequent cases of family cluster infections defined social contact-based transmission as the most probable in this epidemic outbreak.

Performed microbiological investigations of hospitalized patients revealed 1 case of *Shigella flexneri* in a 4-yr old child. Virological investigation was performed on 18 children aged up to 3 yr. They were tested for group A rotaviruses with ELISA, for genogroup I and II enteroviruses with two-step reverse transcription reaction followed by RT-PCR [7].

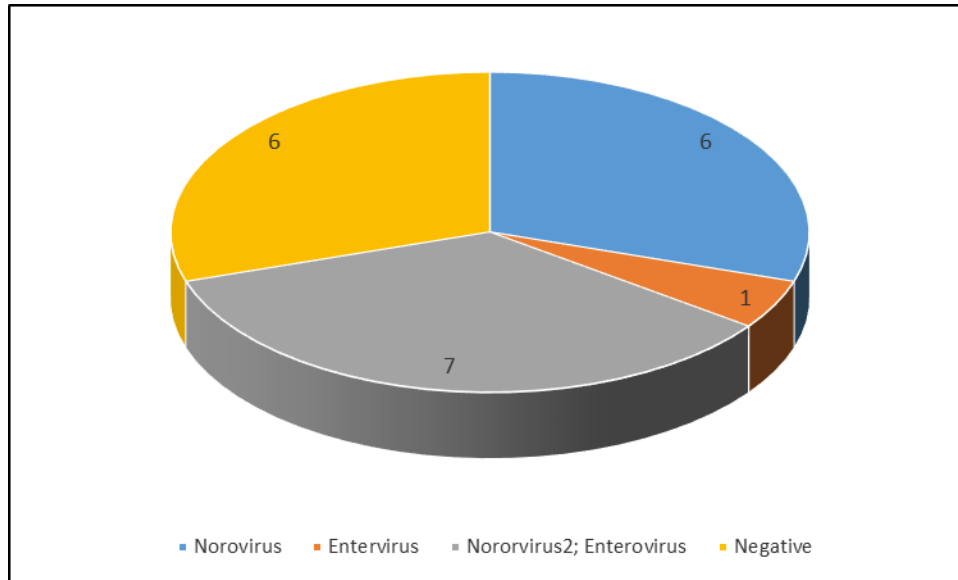


Figure 7 Distribution of revealed causative agents during the period 01.08. – 30.11.2013 by performed virological tests of hospitalized patients at the time of the norovirus epidemic outbreak in the town of Samokov

During the period 06.06. - 10.09.2014, a total of 49 enterocolitis cases were registered in the town of Ihtiman, 43 of which among the Roma population. All patients were town residents. The age group from 0 to 1 yr (15 cases) was the most affected, followed by the one from 1 to 4 yr (14 cases). In all other age groups, single cases were registered.

The sex distribution of cases was 32 males and 17 females.

In the course of the epidemic outbreak, 14 outbreaks, each with 1 case; 2 outbreaks, each with 2 cases; 6 outbreaks, each with 3 cases; 2 outbreaks, each with 4 cases and 1 outbreak with 5 cases were registered.

Performed investigations did not reveal microbiological or virological causative agents. Transmission and spread of infection was social contact-based.

During the same period, this time on the town of Samokov territory, during the period 01.07 - 10.09.2014, 35 enterocolitis cases were registered, 32 of which among the Roma population. All patients were Samokov residents. The age group from 0 to 1 yr (14 cases) was the most affected, followed by the one from 1 to 4 yr (9 cases). In all other age groups, single cases were registered. The sex distribution of cases was 14 males and 21 females. In the course of the epidemic outbreak, 33 outbreaks, each with 1 case and 2 outbreaks, each with 2 cases were registered.

Out of 355 actively traced patients' contact persons, 120 underwent virological investigation, all with negative results.

The latest registered outbreak on the Sofia Province territory was in 2016. During the period 23.03-24.03.2016, 48 students from the Professional High School of Computing and Technology Systems in the town of Pravets were infected. [8] Clinical complaints started on 22.03.2016 and the early hours of 23.03.2016, with predominant nausea, vomiting and pain in the stomach area. Some of the patients also had loose stools without admixtures. The students were from 14 to 19 yr of age. They were from different populated places but lived in the dormitories of the Professional High School of Computing and Technology Systems in the town of Pravets and had meals both in the canteen and elsewhere. Epidemiological investigation revealed that 7 of the infected students had not had meals in the canteen neither at lunch, nor at dinner. The ratio of infected students was 13.5% of the 354 ones living in the dormitory. There were no infected students in the town of Pravets and its vicinity.

Epidemiological investigation performed on 22 students from the Professional High School of Computing and Technology Systems in the town of Pravets who simultaneously exhibited clinical signs of severe gastroenteritis and

were hospitalized in Prof. Ivan Kirov Specialized Hospital for Active Treatment of Infectious and Parasitic Diseases, revealed that the patients' average age was 16 yr, in the range 14-18 yr, of them 17 boys (77%) and 5 girls (23%). [8] The diagnosis was clinic-epidemiological and etiological that was made by testing of fecal samples from the patients for pathogenic intestinal bacteria - Salmonella, Shigella, E. Coli as well as virological that was made by PCR for Norovirus of fecal samples.

Performed diagnostics of the 22 patients including investigation of fecal samples for intestinal bacteria and viruses revealed Norovirus infection in 17 of them that was verified via PCR. Other causative agents (Salmonella, Shigella, E. coli, Campylobacter) were not verified in the fecal samples [8].

Taking into account the microbiological and virological findings as well as the short incubation period, this epidemic outbreak was of norovirus nature.

The annual distribution of norovirus gastroenteritis cases in Sofia Province during the period 2007-2022 is presented in Table 1. Statistical analysis with the Mann-Kendall test does not reveal a distinct monotonic trend in the number of registered infections. Consequently, additional studies are necessary for monitoring of norovirus presence in the region.

Table 1 Annual distribution of norovirus gastroenteritis cases in Sofia Province during the period 2007-2022

Year	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Number of cases	28	21	0	0	0	9	13	0	0	17	0	0	0	0	0	0

For the purpose of comparison, the annual distribution of rotavirus gastroenteritis cases in Sofia Province during the period 2012-2022 is presented in Table 2. The information is taken from the national system for registration of infectious diseases which started reporting on rotavirus gastroenteritis cases in 2012. Statistical analysis with the Mann-Kendall test reveals a stable trend in the number of these infections.

Table 2 Annual distribution of rotavirus gastroenteritis cases in Sofia Province during the period 2012-2022

Year	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Number of cases	86	55	63	96	72	74	57	62	0	0	0

4. Conclusion

The conducted epidemiological study of 13 viral gastroenterocolitis epidemic outbreaks, distinguished by their intensity, scope, etiological and clinical diversity in a region neighboring with the capital of Bulgaria and having specific geographical, economic, ethnical and social characteristics, was the first generalized study in this regard. Currently, the national system for registration of infectious diseases does not report cases identified as norovirus infections.

The norovirus gastroenteritis epidemic outbreaks in Sofia Province were the first considered and described chronologically in the country. They reveal that norovirus infection is a current problem for public healthcare, requiring additional explanations of its spread in modern times as well as efforts for design of new and efficient preventive strategies for its mitigation.

During the period December 2019 and April 2022. no gastroenteritis caused by norovirus infections has been proven in the Sofia Province. The authors believe that this might be due to the lowered search criteria, redirection of resource, the imposed anti-epidemic measures and restrictions during the course of the COVID-19 pandemic.

Compliance with ethical standards

Disclosure of conflict of interest

There is no conflict of interests to be reported.

Statement of informed consent

No patients were directly engaged in setting the research question or the outcome measures, nor were any patients involved in the study's design or implementation. There are no plans to disseminate the results of the research directly to study participants or the relevant patient cohorts.

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