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ABSTRACT
of the dissertation for the degree of Doctor of Philosophy

ETYMOLOGY OF NOROVIRUS INFECTION IN CHILDREN AND IMPROVEMENT OF ITS DIAGNOSTIC METHODS

Specialty: 2414.01 - “Microbiology”

Field of science: Medicine

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GENERAL CHARACTERISTICS OF THE RESEARCH

Relevance of the research. "Acute viral gastroenteritis (AVG) is a significant global health concern, causing 1.45 million deaths each year[1,2,3]. Epidemiological studies indicate that over the past decade, acute viral gastroenteritis outbreaks, including epidemics predominantly caused by viral agents, have been reported across many regions of the world. The proportion of viral gastrointestinal infections (VGIs) in the structure of acute intestinal infections (AII) ranges from 20% to 70% [4,5,6] .

The causative agents of viral acute gastroenteritis (VAG) are reported to include rotaviruses, noroviruses, sapoviruses, adenoviruses, and human astroviruses[7]. Among the etiological factors of viral diarrhea, noroviruses rank second in prevalence after rotaviruses[8]. These viruses often cause outbreaks in children's groups

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[1] Архипов Г.С., Кириллова Е.Н., Архипова Е.И. Заболеваемость острыми кишечными инфекциями вирусной этиологии (ротавирусы, астровирусы, норовирусы) на территории Новгородской области за 2013-2018 гг. // Вестник Новгородского Государственного Университета, 2019, № 1 (113), с.56-59.

[2] Капустин Д.В., Хохлова Н.И., Краснова Е.И. и др. Современные аспекты острого гастроэнтерита вирусной этиологии // Journal of Siberian Medical Sciences, 2019, № 2, p. 106-117.

[3] Bányai K., Estes M., Martella V., Parashar U. Viral gastroenteritis // Lancet. 2018 Ju 14;392(10142): 175-186

[4] Florez I., Nino-Serna L., Beltran-Arroyave C. Acute infectious diarrhea and gastroenteritis in children // Curr Infect Dis Rep. 2020;22

[5] Mokomane M.,Kasvosve L.,de Melo E.et The global problem of childhood diarrhoeal disaeases:emerging strategies in prevention and management \\ Ther.Adv.Infect. Dis.,2018,5(1),p.29-43

[6] Баранов А.А., Намазова-Баранова Л.С., Таточенко В.К. и др. Ротавирусная инфекция у детей - нерешенная проблема // Педиатрическая фармакология. 2017, № 4, с. 248-257.

[7] Хохлова Н.И.,Капустин Д.В.,Краснова Е.И.,Извекова И.Л.,Норовирусная инфекция (Обзорлитературы)// Журнал инфектологии,2018,т.10,№1,с. 5-14.

[8] Lekana-Douki S., Kombila-Koumavor C., Nkoghe D. et al. Molecular epidemiology of enteric viruses and genotyping of rotavirus, adenovirus and astrovirus among children under 5 years old in Gabon // Int. J. Infect. Dis., 2015, 34, p.90-95.

and are one of the main causes of hospital-acquired infections.

In many cases, these viruses are coincidentally detected together in the same patient. According to data from various authors, 18% of all cases of acute gastroenteritis in children as a monoinfection, while in combination with other intestinal viruses and bacteria, they account for 40% [9,10].

Among all viral agents causing diarrhea diseases, noroviruses account for 34-69.1% in the setting of multi-profile pediatric hospitals. The literature does not provide clear information on which age groups are most susceptible to norovirus infection. Some studies indicate that older children and adults are more commonly affected, while others find that children under the age of 2 are more frequently infected, accounting for 64% of all cases[11,12,13]. O.I. Petrov and his colleagues note that norovirus infections are most prevalent in children during their first year of life, but are also commonly seen in adults, particularly those aged 20 to 30[14].

The higher incidence of norovirus infections during the winter months, combined with its resemblance to rotavirus infection,

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[9] Atmar R., Ramani S., Estes M. Human noroviruses: recent advances in a 50-year history // Curr Opin Infect Dis. 2018 Oct;31(5):422-432

[10] Randazzo W, D'Souza D, Sanchez G. Norovirus: The Burden of the Unknown // Ad\ Food Nutr Res. 2018:86:13-53

[11] .Пронько Н.В., Красько Ю.П.Норовирусная инфекция:Особенности эпидемиологии и клинико- лабараторных проявлений на современном этапе//Актуальная инфектология,2017,т.5,№1,с.14-17.

[12] Lee H., Lee J., Kim S. et al. Correlation between changes in microbial / physicochemical properties and persistence of human norovirus during cabbage Kimchi fermentation // J. Microbiol. Biotechnolog., 2017, 4, p.1707-1770.

[13] Rouhani S., Yori P., Olortegui M. et al. Etiology, Risk Factors, and Interactions of Enteric Infections and Malnutrition and the Consequences for Child Health and Development Project (MAL-ED) Network Investigators. Norovirus infection and acquired immunity in 8 countries: results from the MAL-ED study // Clin Infect Dis., 2016, 62(10), p.1210-1217

[14] Петров М.С., Попова О.П., Заикин В.Л. и др. Клиническая характеристика норовирусной инфекции у детей / Материалы Российской научно практической конференции инфекционных Болезней ВМА им. С.М. Кирова. СПб., ВМедА. 2006, 340 с.

underscores the importance of accurately distinguishing between the two[15].

The purpose and objectives of the research. The aim of the study is to investigate the serological and epidemiological characteristics of mono- and mixed norovirus intestinal infections among children in modern conditions and to assess the effectiveness of diagnostic methods.

To accomplish this, the following objectives were pursued.

1. Serological detection of norovirus antigen through diagnostic methods in a group of children suspected of having gastrointestinal infections with an unknown etiology;
2. Determining the frequency of mono-norovirus gastrointestinal infections in children across different age and gender groups;
3. Assessing the prevalence of mixed norovirus gastrointestinal infections (co-infected with rotavirus and adenovirus) in children of various age and gender groups;
4. Investigating the epidemiological features of mono-norovirus gastrointestinal infections in children;
5. Study the epidemiological features of mixed norovirus gastrointestinal infections in children.
6. Determining the risk groups and factors associated with mono- and mixed norovirus gastrointestinal infections in children.

Scientific novelty of the dissertation. In Azerbaijan, the role of noroviruses as an etiological factor in intestinal infections of unknown etiology among children has remained virtually unstudied. The incidence rate of mono- and mixed-norovirus intestinal infections among children has been determined, and the microbiological diagnosis of these infections (along with Group A rotavirus and adenovirus serotypes 40/41) has been conducted. Certain epidemiological characteristics (such as age,

[15] Lopman B., Steele D., Kirkwood C., Parashar U. The vast and varied global burden of norovirus: Prospects for prevention and control // PLOS Med. 2016;13(4):e1001999

gender, monthly and seasonal distribution, intra-annual and multi-year dynamics) have been examined. The effectiveness of immunochromatographic and enzyme-linked immunosorbent assay (ELISA) methods in the serological diagnosis of norovirus intestinal infections has been evaluated.

Practical significance of the dissertation work. The study has clarified the role of noroviruses as an etiological agent of gastrointestinal infections of unknown origin among children under modern conditions. It has determined the prevalence of noroviruses in both mono-infections and in association with other intestinal viruses, such as group A rotaviruses and adenoviruses of serotypes 40/41. The epidemiological features of both mono- and mixed norovirus infections have also been examined. The important microbiological and epidemiological data obtained can be used in the microbiological diagnosis and epidemiological surveillance of virus-induced diarrheas among children, as well as norovirus intestinal infections. The appropriateness of using the immunochromatographic method in the serological diagnosis of norovirus intestinal infections has been demonstrated.

Approbation of the research. The main provisions of the dissertation were presented and discussed at the 9th International Mardin Artuklu Scientific Research Conference (January 20-22, 2023, Mardin, Turkey), the 10th Eurasian International Scientific Research Approaches Congress (February 16-17, 2023, Baku), the 12th International Scientific Research Conference (February 2023, Baku), and the International Scientific-Practical Conference on "Current Issues of Medical Prevention" dedicated to the 100th anniversary of National Leader Heydar Aliyev (October 27, 2024, Baku). The preliminary discussion of the dissertation was held at the meeting of the Scientific Council of Odlar Yurdu University on May 8, 2024 (protocol No 8).

Published works.

A total of 12 proceedings have been published on the dissertation topic, including 8 scientific articles (1 of which are indexed in the Scopus international database) and 5 abstracts (2 of which are included in the proceedings of international conferences).

Key points presented for defense:

- Norovirus gastrointestinal infections play a significant role in the structure of acute gastrointestinal infections.
- Norovirus gastrointestinal infections are recorded both as mono-infections and mixed infections.
- The study of the epidemiological characteristics of norovirus gastrointestinal infections allows for the identification of risk groups and risk factors.

Volume and Structure of the Dissertation:

The dissertation consists of 137 pages (176716 characters) of computer-typed text and includes the following sections: Table of Contents (788 characters), Introduction (6,238 characters), Chapter I (43983 characters), Chapter II (2631 characters), Chapter III (28555 characters) and Chapter IV (19593 characters), Discussion of the Results (27653 characters), Conclusion (42449 characters), Results (3802 characters), Practical Recommendations (1024 characters), and the list of references.

The dissertation is illustrated with 5 tables and 20 graphs. The list of references includes 265 sources, among them 12 in Azerbaijani, 134 in Russian, and 119 in other foreign languages.

MATERIALS AND METHODS

The research was conducted from 2018 to 2020 at the Enterovirus Infections Laboratory of the Scientific Research Institute of Medical Prevention named after V.Y. Akhundov. Fecal samples collected from children aged 0-18 years, who were admitted to various pediatric hospitals in Baku with a diagnosis of "gastrointestinal infection of unknown etiology," were examined for certain intestinal viruses—rotaviruses, adenoviruses, and noroviruses—using serological methods. In total, 411 child patients were examined: 59 samples (14.4%) were collected in January-December 2018, 293 samples (71.3%) in January-October 2019, and 59 samples (14.4%) in February-March 2020.

The age distribution of the examined children was as follows: 93 children (22.6%) were under 1 year old, 129 children (31.4%) were between 1-3 years old, 98 children (23.8%) were between 3-7 years old, and 91 children (22.1%) were over 7 years old. Among the total number of examined children, 219 (53.3%) were boys and 192 (46.7%) were girls. Over the 3-year study period (2018-2020), the epidemiological features of certain viral gastrointestinal infections were analyzed within each calendar year, while the study of the epidemiological features of astrovirus gastrointestinal infections was carried out both within the epidemic year and throughout the calendar year.

The prevalence of certain viral gastrointestinal infections, both in mono- and mixed forms, along with their age, gender characteristics, annual dynamics, monthly detection rates, and seasonality, were examined. Group A rotavirus, adenovirus serotype 40/41, and norovirus antigens were identified using immunochromatography and enzyme-linked immunosorbent assay (ELISA) methods.

Immunochromatographic testing was performed using the Certest Biotec (Spain) test system, while the enzyme-linked immunosorbent assay (ELISA) for detecting antigens of group A rotavirus, adenovirus serotype 40/41, and norovirus in fecal samples was carried out using the solid-phase "sandwich" test system (R-Biopharm, RIDASCREEN, Germany). The tests were conducted according to the manufacturer's guidelines.

Descriptive-evaluative and analytic epidemiological research methods were applied in studying the epidemiological characteristics of viral gastrointestinal infections.

Statistical Analysis of the Results

The statistical analysis of the results was conducted using the SPSS-26 software package. The accuracy of differences between independent groups was assessed using the Mann-Whitney U test. Additionally, the evaluation of statistical significance of the results was performed using Fisher's exact test and qualitative variance analysis.

The statistical significance of differences between the qualitative features of the examined groups was assessed using the χ^2 test and Fisher's exact test. A significance level of $p<0.05$ was considered statistically significant [41-43].

RESULTS AND DISCUSSION

Before discussing the epidemiological features of mono-norovirus gastrointestinal infections in children, it is important to highlight the overall findings concerning various intestinal viruses (group A rotavirus, adenovirus serotype 40/41, norovirus, and HAstV) in the 411 child patients examined. Among the study group, 114 children (27.7%) showed no presence of the studied intestinal viruses, while 297 children (72.3%) tested positive for one or more intestinal viruses.

Of the total, 153 children (51.5%) were diagnosed with mono-virus gastrointestinal infections, while 144 children (48.5%) had mixed-virus gastrointestinal infections. Within the mixed-virus infections, two-virus associations were found in 29.7% (122 children), and three-virus associations in 5.4% (22 children).

The distribution of mono-virus infections over the years was as follows: in 2018, 25 children (54.3±7.3%); in 2019, 109 children (51.9±3.4%); and in 2020, 19 children (46.3±7.8%). The prevalence of mixed-virus infections was 45.7±7.3% (21 children) in 2018, 43.1±3.4% (101 children) in 2019, and 53.7±7.8% (22 children) in 2020.

The breakdown of individual viruses identified included:

- Group A rotavirus in 97 children (23.6%),
- Adenovirus serotype 40/41 in 120 children (29.2%),
- Noroviruses in 246 children (59.9%).

A comprehensive analysis was conducted on the prevalence of mono-virus gastrointestinal infections in children throughout the study period (2018), focusing on factors such as age, gender, monthly trends, seasonality, and the etiological agents. In 2018, the prevalence of mono-virus gastrointestinal infections was 54.3±7.3%, 71.6±3.9% in 2019, and 51.9±3.4% during the first two months of 2020 (February-March).

When analyzing the prevalence of mono-virus gastrointestinal infections by age, it was found that the incidence in children under 1 year old was 11.9±2.8%, while the 1-3 age group showed nearly three times higher rates at 38.1±4.2%. The highest prevalence of mono-virus infections occurred in the 1-3-year-old group. For the 3-7-year-olds, the rate was 29.9±4.0%, and for those over 7 years, it was 20.1±3.5%. The peak prevalence of mono-virus infections was observed in the 1-3-year-old group, with a rate of 38.1±4.2%.

Gender-wise, the prevalence of mono-virus gastrointestinal infections was higher in boys (56.0±4.3%) compared to girls (44.0±4.3%).

The monthly dynamics revealed no infections in August. The highest rates of infection were detected between February and May, with prevalence ranging from 12.7±2.9% to 15.7±3.1%. The lowest infection levels were seen in the fall-winter months, with rates ranging from 0.7±0.7% to 6.7±2.2%.

Seasonal analysis indicated that the lowest prevalence of mono-virus infections occurred in the fall (9.7±2.6%), with the highest levels recorded in the spring at 42.5±4.3%. Winter also showed significant prevalence, with a rate of 29.1±3.9%.

In terms of the etiological agents, the prevalence of group A rotavirus was 23.6±2.1%, adenovirus serotype 40/41 was found in 29.2±2.2%, and noroviruses were identified in 59.9±2.4% of cases. Among these, adenovirus serotype 40/41 had the highest prevalence (Figure 1).

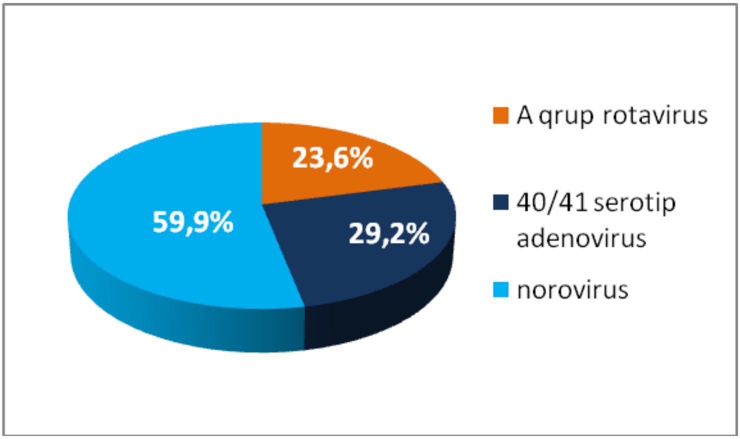

Figure 1. Etiological Structure of Mono-Virus Gastrointestinal Infections in Children

An epidemiological analysis was performed to assess the prevalence of mono-virus gastrointestinal infections in the pediatric population, considering variables such as gender, age groups, months, and seasons. The distribution of children by age in the study was as follows:

- In 2018, the age rate was: Under 1 year: 3.2±1.8%: 1-3 years: 2.3±1.3%: 3-7 years: 26.5±4.5%; Over 7 years: 29.7±4.8%
- In 2019, the age rate was:Under 1 year: 87.1±3.5%;1-3 years: 80.6±3.5%; 3-7 years: 56.1±5.0%; Over 7 years: 58.2±5.2%
- For the first two months of 2020, the age rate was:Under 1 year: 9.7±3.1%;1-3 years: 17.1±3.3%;3-7 years: 17.3±3.8%; Over 7 years: 12.1±3.4%

In terms of gender distribution across age groups, the results were as follows:

- Among boys:Under 1 year: 49.5±5.2%;1-3 years: 55.0±4.4%;3-7 years: 59.2±5.0%;over 7 years: 48.4±5.2%
- Among girls:Under 1 year: 50.5±5.2%;1-3 years: 45.0±4.4%;3-7 years: 40.8±5.0%;over 7 years: 51.6±5.2%

These findings highlight the gender distribution across various age groups, offering insights into the demographic patterns of children affected by mono-virus gastrointestinal infections.

The prevalence of mono-virus gastrointestinal infections in children, based on age groups, revealed that the occurrence of a single viral pathogen was as follows:

- among the children under 1 year: 26.1±3.6%
- In the 1-3 year age group: 28.8±3.7%
- In the 3-7 year age group: 20.9±3.3%
- Among the children over 7 years: 24.2±3.5%

The study of the etiological agents of mono-virus gastrointestinal infections in children, focusing on group A rotavirus, adenovirus serotype 40/41, and norovirus, showed the following prevalence:

- Group A rotavirus infection: Under 1 year: 14 children (15.1±3.7%); 1-3 years: 40 children (31.0±4.1%) ;3-7 years: 25 children (25.5±4.4%); Over 7 years: 18 children (19.8±4.2%);

40/41 serotype adenovirus infection: Under 1 year: 17 children (18.3±4.0%);1-3 years: 47 children (36.4±4.2%) ; 3-7 years: 36 children (36.7±4.9%) ; Over 7 years: 20 children (22.0±4.3%)

These findings indicate the distribution of various viral pathogens in relation to age groups and provide insights into the epidemiology of mono-virus gastrointestinal infections in children.

Norovirus gastrointestinal infections were recorded in 48 children under 1 year old (19.5±2.5%), 87 children in the 1-3 years age group (35.4±3.0%), 64 children in the 3-7 years age group (26.0±2.8%), and 47 children over 7 years old (19.1±2.5%). Overall, the prevalence of gastrointestinal infections caused by the aforementioned viral pathogens was as follows: under 1 year – 19.2±2.3%, 1-3 years – 35.4±2.8%, 3-7 years – 25.6±2.5%, and over 7 years – 19.9±2.3% ($p<0.001$).

Noroviruses were the most common etiological agents of mono-virus gastrointestinal infections in the studied pediatric cohort, followed by adenovirus serotype 40/41 and group A rotavirus. The highest prevalence of viral gastrointestinal infections was observed in the 1-3 years age group – 35.4±2.8%. The lowest prevalence was observed in children under 1 year old – 19.2±2.3% ($p<0.001$).

Overall, the incidence rate of intestinal infection, in which noroviruses have been confirmed as the etiological factor, is reflected in Figure 2.

Before analyzing the gender-based distribution of mono-virus gastrointestinal infections among children, the gender composition of the examined children was assessed. In 2018, 4.6% of the children in the study were boys, and 14.1% were girls. In 2019, boys accounted for 68.9% and girls for 74.0% of the examined children. During the first two months of 2020, 16.4% of the children examined were boys, and 12.0% were girls.

Overall, 219 boys (53.3%) and 192 girls (46.7%) were included in the study.

The investigation of viral gastrointestinal infections based on gender showed that the prevalence of viral gastrointestinal infections was 55.2±2.9% (131 boys) among boys, and 44.8±2.9% (133 girls) among girls. Mono-virus gastrointestinal infections, involving a single virus, were identified in 81 boys (52.9±4.0%) and 72 girls (47.1±4.0%).

In %

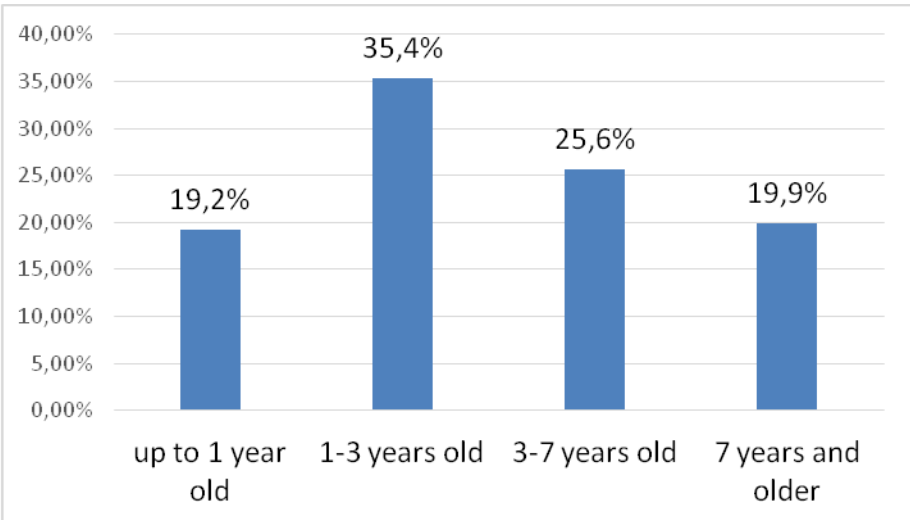

Figure 2. Prevalence of Viral Gastrointestinal Infections Across Different Age Groups

The results regarding the prevalence of different viral gastrointestinal infections based on gender are presented in Table 1.

Table 1 shows that the prevalence of intestinal infections caused by serotype 40/41 adenovirus and norovirus among boys was the highest compared to other intestinal viruses in both boys and girls, at 56.1±3.2% and 43.9±3.2%, respectively.

In terms of prevalence, serotype 40/41 adenovirus ranked second, with rates of 32.9±3.2% in boys and 2.5±3.1% in girls. Overall, mono-viral intestinal infections were observed in 52.9±4.0% of boys and 47.1±4.0% of girls.

Among the children examined in 2018, A group rotavirus intestinal infections were the most common, accounting for 27.1%. However, in 2019, norovirus intestinal infections dominated among viral intestinal infections, with a prevalence of 71.3±2.2%. In 2020, A group rotavirus intestinal infections once again had a significant share in the structure of viral intestinal infections among children, with a prevalence of 33.9%.

Table 1

The prevalence of various viral gastrointestinal infection based on gender among the children

№	Gender	A group rotavirus		40/41 serotip adenovirus		Norovirus
		Abs. number	%±m	Abs. number	%±m	Abs. number
1	Boys	50	22,8±2,8	72	32,9±3,2	138
2	Girls	47	24,5±3,1	48	25,0±3,1	108

Over a three-year study period, the frequency of viral intestinal infections among children remained nearly consistent in 2018 and 2020, at 15.5±2.1% and 13.8±2.0%, respectively. However, a significant increase in the incidence rate was observed in 2019, reaching 70.7±2.6%.

Examining mono-viral intestinal infections—those caused by a single specific intestinal virus—revealed varying frequencies across the years: 16.3±3.0% in 2018, a peak of 71.2±3.7% in 2019, and a decline to 12.4±2.7% in 2020. Mono-viral infections were most prevalent in 2019 (71.2±3.7%) and least common in 2020 (12%).

Understanding the seasonal patterns of mono-viral intestinal infections is critical, as it provides insight into the epidemic process and helps identify seasonal risk factors, enabling effective epidemiological control.

To study the seasonal distribution of these infections, the children were grouped by season: 127 children in winter (December–February), 188 in spring (March–May), 55 in summer (June–August), and 41 in autumn (September–November).

The detection rates of infections caused by specific intestinal viruses, such as group A rotavirus, 40/41 serotype adenovirus, and norovirus, varied by season: Winter: 30.9±2.3%, Spring: 45.8±2.5%, Summer: 13.4±1.7%

Autumn: 10.0±1.5%

These findings indicate that viral intestinal infections were most frequently observed in winter and spring (30.9%–45.7%) and were least common in autumn. Within this framework, mono-viral infections had the highest detection rate in spring (45.7±2.5%) and the lowest in autumn (10.0±1.5%).

Group A rotavirus intestinal infections in children were detected throughout the year, with the highest incidence recorded in spring (25.5±3.2%) and the lowest in winter (21.3±3.6%). In general, these infections displayed a distinct spring-summer seasonality among children.

An analysis of the seasonal distribution of 40/41 serotype adenoviral intestinal infections in the pediatric population showed that the highest detection rate occurred in summer (34.5±6.4%), while the lowest was in autumn (24.4±6.7%).

For norovirus intestinal infections in children, the seasonal detection frequency analysis indicated that the highest incidence was in spring (46.7±3.2%), whereas the lowest was in autumn (11.4±2.0%). Interestingly, noroviral infections were nearly equally frequent in summer and autumn, with detection rates of 11.8±2.1% and 11.4±2.0%, respectively (Fig. 3)

The monthly intra-annual trends of general viral intestinal infections in children reveal two prominent epidemic peaks: one in February and another in August. The February peak reached 62.5±6.5%, while the August peak was significantly higher, reaching 100.0%.

Both epidemic cycles lasted two months, but the second cycle in August exhibited a much greater amplitude. Morbidity rates for general viral intestinal infections showed a decline starting in February, followed by a relatively steady increase from April. After peaking in August, the rates began to drop, with a slight increasing observed in November.

Overall, the monthly dynamics of viral intestinal infection morbidity demonstrate a distinct two-wave epidemic pattern.

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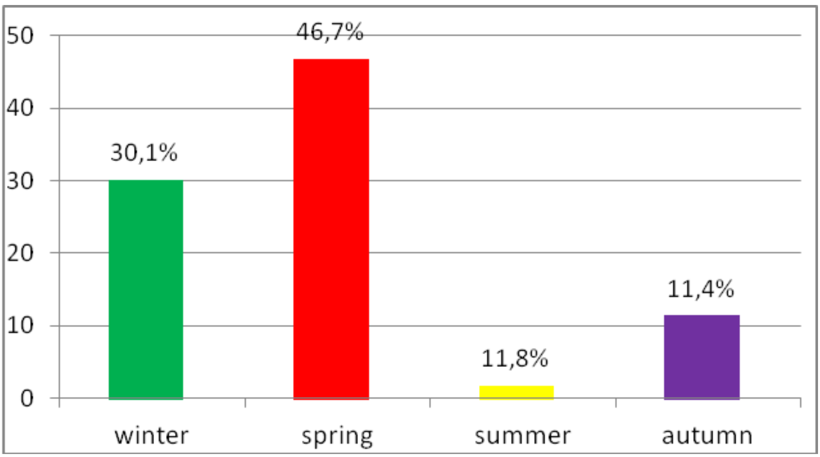

Figure 3 Seasonal distribution of norovirus intestinal infection frequency among children

The primary difference is that the extensive indicators for single-virus infections are roughly half as high.

As illustrated in Figure 10, the epidemic process for single-virus viral intestinal infections among children features two distinct peaks (cycles). The first peak occurs in February at 33.9±6.3%, while the second peak appears in July at 48.1±9.6%.

The first epidemic cycle lasts two months, while the second extends over three months. From February, the extensive indicators for single-virus infections decline and stabilize at relatively low levels through March, April, and May. Beginning in May, the indicators gradually increase, reaching their second peak in July, followed by a plateau lasting three months. Starting in November, there is a noticeable and steady decline in these indicators, continuing through the end of the year.

This pattern highlights the distinct winter-summer seasonality of both general viral intestinal infections and those caused by a single virus among the studied children. The intensity of the epidemic process during these seasons may be influenced by factors such as the proportion of specific intestinal viral infections, the role of intestinal viruses as causative agents, and the age distribution of the affected population.

The epidemic process of group A rotavirus intestinal infections among children has been highly dynamic. Throughout the year, fluctuations in the incidence of these infections, with periods of both increase and decrease, were observed. The pattern of the epidemic process followed a zigzag trajectory (with repeated short spikes). Four epidemic peaks and four periods of decline in the incidence of group A rotavirus infections were recorded. The epidemic process was marked by recurring cycles of increase and decrease in incidence across nearly all seasons. Four distinct infection cycles were identified: the first cycle occurred in January at 36.4±14.5%, the second in September at 25.9±8.4%, and the fourth in November at 28.6±12.1%. The first, second, and fourth peaks lasted for two months, while the third peak lasted for three months.

The analysis of the monthly dynamics of norovirus intestinal infections in children revealed that the epidemic process for norovirus infections also follows a cyclical pattern, with epidemic increases and decreases occurring throughout the year across all seasons (Fig. 4).

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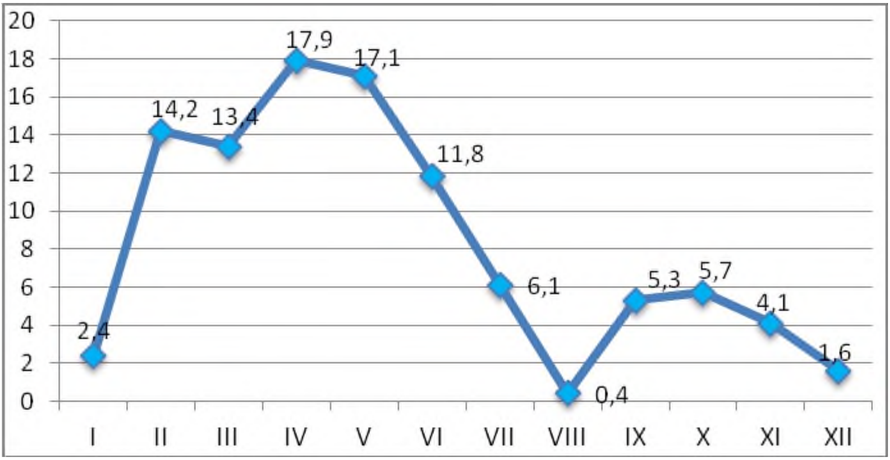

Figure 4. Average intra-annual monthly dynamics of norovirus intestinal infections among children

Of the four recorded epidemic cycles, two were high-amplitude, and one was low-amplitude. Norovirus-related intestinal infections among children began to rise in February, with the first epidemic peak reaching 14.2±2.2%. The infection rate increased more gradually in March, culminating in a second peak in April at 17.9±2.4%.

The third cycle, characterized by moderate amplitude, occurred in June with an infection rate of 11.8±2.1%. Following this, rates began to rise again in July, reaching 5.3±1.4% in September and 5.7±1.5% in October. Each epidemic cycle of norovirus-related intestinal infections lasted two months.

A comparison of the epidemic trends for intestinal infections caused by group A rotavirus, adenovirus serotypes 40/41, and norovirus in children reveals distinct differences. In August, group A rotavirus infections were not detected, while adenovirus serotypes 40/41 infections peaked at 100.0%. Meanwhile, only one case of norovirus infection was recorded, with an incidence rate of 0.4±0.4%.

Norovirus-related intestinal infections, similar to those caused by adenovirus serotypes 40/41, exhibit a pronounced winter-summer seasonality, which is especially significant.

Over the study period, two-virus associations were identified in 2018 in 17 individuals (28.8±5.9%) and three-virus associations in 4 individuals (6.8±3.3%). In 2019, two-virus associations were detected in 86 cases (29.4±2.7%) and three-virus associations in 15 cases (5.1±1.3%). In 2020, two-virus associations were found in 19 children (32.2±6.1%) and three-virus associations in 3 children (5.1±2.9%).

In 2018, the most common two-virus combinations were RV+NV, identified in 12 cases (20.3±5.2%), AdV+NV in 11 cases (18.6±5.1%), and RV+AdV in 6 cases (10.2±3.9%). Among three-virus associations, the RV+AdV+NV combination was observed in 4 cases (6.8±3.3%).

In 2019, two-virus associations included RV+NV in 46 cases (15.7±2.1%), AdV+NV in 61 cases (20.9±2.4%), and RV+AdV in 24 cases (8.2±1.6%). Three-virus associations were confirmed in 15 cases (5.1±1.3%).

In 2020, the RV+NV combination was recorded in 9 cases (15.3±4.7%), AdV+NV in 14 cases (23.7±5.5%), and RV+AdV in 5 cases (8.5±3.6%). The RV+AdV+NV three-virus association was identified in 3 cases (5.1±2.9%).

Two-virus associations were least common in children under 1 year of age (12.9±3.5%) and most frequent in the 1–3-year age group (41.1±4.3%). The highest detection rate of three-virus mixed infections (6.2±2.1%) was also observed in the 1–3-year age group. Among children under 1 year and those aged 3–7 years, three-virus associations occurred at nearly the same frequency—5.4±2.3% and 5.1±2.2%, respectively. The lowest frequency of three-virus associations was noted in children over 7 years of age (4.4±2.1%).

The distribution of two- and three-virus mixed intestinal infections among children based on gender is shown in Figure 4.

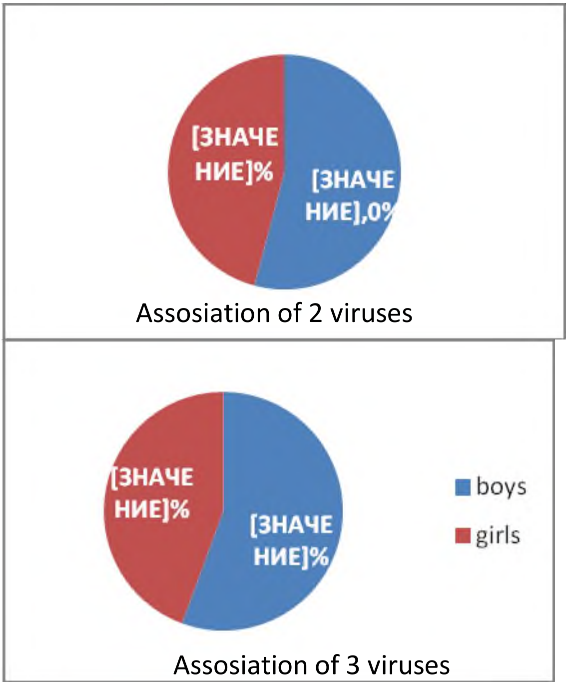

Figure 5. Gender-Based Frequency Distribution of Two- and Three-Virus Associations Among Children

As shown in Figure 5, both two-virus and three-virus associations were more commonly observed among boys, with rates of 32.0±3.2% and 5.9±1.6%, respectively. Among girls, three-virus associations were less frequent, recorded at 4.7±1.5%.

The highest incidence of two-virus mixed intestinal infections among children occurred during autumn (34.1±7.4%), while the lowest was in winter (28.3±4.0%). Overall, two-virus associations were predominantly observed in the summer and autumn seasons, with rates of 32.7±6.3% and 34.1±7.4%, respectively.

For three-virus mixed intestinal infections, the highest frequency was recorded in spring (6.9±1.9%), whereas the lowest was in winter (5.5±2.0%). Only one case of three-virus associations was documented during the summer (1.8±1.8%) and autumn (2.4±2.4%) seasons.

The incidence of two-virus associations showed a sharp increase during the winter-autumn seasons, along with a gradual rising trend during spring and summer. The epidemic process consisted of three peaks (cycles): two high-amplitude and one moderate-amplitude. The first peak was in February (32.1±6.2%), the second in July (33.3±9.1%), and the third in December (40.0±21.9%). Overall, the incidence of two-virus associations remained high in the first half of the year and exhibited a steady upward trend in the second half. Notably, similar rates were observed in March (26.7±5.7%) and April (26.8±5.3%), indicating a predominance of two-virus associations during the winter-autumn seasons.

For three-virus associations, no cases were detected in July, August, October, or November. The highest incidence occurred in December (20.0±17.9%), while the lowest was in February (3.6±2.5%). Intermediate rates were recorded in May (8.7±3.4%) and March (6.7±3.2%). Although no clear seasonal pattern was evident for three-virus associations, the peak incidence was observed in winter (20.0±17.9%). Both two-virus and three-virus associations reached their highest levels during the winter season.

The primary risk group for mixed viral intestinal infections in children was found to include those aged 1–3 years (58.1±4.1%) and boys (50.6±3.9%). The risk factors for mixed virus infections, based on etiological agents, were the two-virus associations RV+AdV and RV+NV, with risks of 10.9±2.7% and 21.7±3.6% in the 1-3 age group, respectively. The risk factor for mixed virus infections with two-virus associations was highest in the autumn (34.1±7.4%), while for three-virus associations, it was highest in the spring (6.9±1.9%).

An analysis of the etiological agents involved in two- and three-virus mixed intestinal infections among children identified group A rotaviruses, adenovirus serotypes 40/41, and noroviruses as key contributors. These findings are shown in the following diagram.

In two-virus associations, noroviruses accounted for the highest proportion (53.9±2.4%), followed by adenovirus serotypes 40/41 (29.2±2.2%) and group A rotaviruses (23.6±2.1%). For three-virus associations, all three viruses—group A rotaviruses, adenovirus serotypes 40/41, and noroviruses—were concurrently detected in 22 children, representing a rate of 5.4±1.1%.

A comparative evaluation of the effectiveness of immunochromatography and enzyme-linked immunosorbent assay (ELISA) methods for diagnosing norovirus intestinal infections in children revealed a 99.0% concordance in norovirus antigen detection results between the two methods.

Norovirus infections had the highest detection rate in the 1-3 age group (35.4±3.0%). These infections were more frequent in boys (56.1±3.2%) than girls (43.9±3.2%). Norovirus infections were most common in the spring (46.7±3.2%) and less common in autumn (11.4±2.0%). The epidemic process for norovirus infection showed a cyclical pattern, with peaks and declines recorded in nearly every season, consisting of two high-amplitude and one low-amplitude cycles.

It is essential to conduct serological testing for the etiological agents of viral intestinal infections, including group A rotavirus, adenovirus serotypes 40/41, and norovirus, in children admitted with a diagnosis of "unknown etiology severe intestinal infections," especially those under 3 years of age.

Serological testing for the etiological agents of viral intestinal infections, including group A rotavirus, adenovirus serotypes 40/41, and norovirus, is recommended to be performed using immunoenzymatic (ELISA) and immunochromatographic methods.

Serological testing for the etiological agents of viral intestinal infections, including group A rotavirus, adenovirus serotypes 40/41, and norovirus, is recommended for children aged 1-3 years who are in the high-risk group, especially during the winter-spring season, which is associated with an increased risk

CONCLUSION

1. 153 cases (51.5%) of mono-virus intestinal infections and 144 cases (48.5%) of mixed virus intestinal infections were recorded during the research. Among the mixed virus infections, two-virus associations accounted for 29.7%, while three-virus associations made up 5.4%. The etiological agents of mono-virus intestinal infections were identified as follows: group A rotaviruses with a detection rate of 23.6%, adenovirus serotype 40/41 with 29.2%, and noroviruses with 59.9% [1,5].
2. Group A rotavirus infections were most commonly found in the age group 31.0±4.1%. The infection rate was higher in girls (24.5±3.1%) compared to boys (22.8±2.8%). These infections were more common in the spring (25.5±3.2%) and less common in winter (21.3±3.6%). The epidemic process for group A rotavirus infection followed a zigzag pattern, with four epidemic peaks and four declines in cases [2,6].
3. The maximum detection rate of adenovirus serotype 40/41 infections was found in the 3-7 age group (36.7±4.9%). These infections were more common in boys (32.9±3.2%) than girls (25.0±3.2%). The highest detection rate occurred in the summer (34.5±6.4%), while the lowest was in autumn (24.4±6.7%). The epidemic process for adenovirus infection displayed an unstable trend with two moderate and two high-amplitude epidemic cycles [8].
4. Norovirus infections had the highest detection rate in the 1-3 age group (35.4±3.0%). These infections were more frequent in boys (56.1±3.2%) than girls (43.9±3.2%). Norovirus infections were most common in the spring (46.7±3.2%) and less common in autumn (11.4±2.0%). The epidemic process for norovirus infection showed a cyclical pattern, with peaks and declines recorded in nearly every season, consisting of two high-amplitude and one low-amplitude cycles [9].
5. The frequency of mixed virus intestinal infections was highest in the 1-3 age group (5.8±4.8%). These infections were more common in boys (50.6±3.9%) than girls (45.9±4.3%). The peak detection rate for mixed virus infections occurred in the spring (49.3±4.3%), and

the epidemic process did not exhibit strong seasonality. In 2018, among two-virus associations, RV+NV was found in 8.5%, AdV+NV in 6.8%, and RV+AdV in 10.2%. The three-virus association RV+AdV+NV was identified in 6.8%. In 2019, the two-virus associations were RV+NV at 5.5%, AdV+NV at 20.8%, and RV+AdV at 8.2%. The three-virus association RV+AdV+NV was found in 5.1%. In 2020, the two-virus associations included RV+NV at 15.3%, AdV+NV at 23.7%, and RV+AdV at 8.5%, while the three-virus association RV+AdV+NV was detected in 5.1% [3,7].

6. The primary risk group for mixed viral intestinal infections in children was found to include those aged 1–3 years (58.1±4.1%) and boys (50.6±3.9%). The risk factors for mixed virus infections, based on etiological agents, were the two-virus associations RV+AdV and RV+NV, with risks of 10.9±2.7% and 21.7±3.6% in the 1-3 age group, respectively. The risk factor for mixed virus infections with two-virus associations was highest in the autumn (34.1±7.4%), while for three-virus associations, it was highest in the spring (6.9±1.9%) [7,11].

7. A comparative evaluation of the effectiveness of immunochromatography and enzyme-linked immunosorbent assay (ELISA) methods for diagnosing norovirus intestinal infections in children revealed a 99.0% concordance in norovirus antigen detection results between the two methods [10].

PRACTICAL RECOMMENDATIONS

1. It is essential to conduct serological testing for the etiological agents of viral intestinal infections, including group A rotavirus, adenovirus serotypes 40/41, and norovirus, in children admitted with a diagnosis of "unknown etiology severe intestinal infections," especially those under 3 years of age.

2. Serological testing for the etiological agents of viral intestinal infections, including group A rotavirus, adenovirus serotypes 40/41, and norovirus, is recommended to be performed using immunoenzymatic (ELISA) and immunochromatographic methods.

3. Serological testing for the etiological agents of viral intestinal infections, including group A rotavirus, adenovirus serotypes 40/41, and norovirus, is recommended for children aged 1-3 years who are in the high-risk group, especially during the winter-spring season, which is associated with an increased risk.

LIST OF PUBLISHED WORKS ON THESIS TOPIC

1. Rüstəmova L.İ., Əliyev M.H., Məmmədova M.N, Babayeva S.F. Kəskin virus qastroenteritlərinin etiologiyasında norovirusların epidemioloji əhəmiyyəti// Azərbaycan təbabətinin müasir nailiyyətləri, 2023, № 1,s.24-28.
2. Рустамова Л.И., Кулиева З.М., Алиев М.Г., Ибадова Т.И., Исаева М.М., Бабаева С.Ф., Мамедова М.Н. Эпидемиологическая характеристика моно вирусной кишечной инфекции у детей в г.Баку // Azərbaycan Perinatologiya və Pediatriya Jurnalı, 2023, т.9, № 1, с.38-44.
3. Babayeva S.F., İsayeva M.M. Uşaqlarda mikst viruslu bağırsaq infeksiyası zamanı epidemik prosesin xüsusiyyətləri // Odlar Yurdu Universitetinin Elmi və pedaqoji Xəbərləri, 2023, № 62, s.213-217.
4. Бабаева С.Ф.Особенности эпидемического процесса моно и микст аденовирусной кишечной инфекции у детей в г.Баку// Sağlamlıq, 2023, cild 32, № 4, c.88-94.
5. Aliyev M.Q., Rustamova L.I., Ibragimova G.Kh., Babayeva S.F. Mono-norovirus intestinal infection in children of early age in Baku, // 9th International Mardin Artuklu Scientific researches conference, January 20-22, 2023,Mardin, Turkey, p.260.
6. Aliyev M.H., Rustamova L.I., Babayeva S.F. Mixed norovirus intestinal infection among early aged children in Baku city//

Euroasia International Congress on Scientific researches and recent trends, February 16-17, 2023, Baku, Azerbaijan, p.338-339.
7. Əliyev M.H., Rüstəmova L.İ., Babayeva S.F. Bakı şəhərində erkən yaşlı uşaqlar arasında mikst norovirus bağırsaq infeksiyası// XIII Beynəlxalq elmi araşdırmalar konfransı. Elmi Tədqiqat Beynəlxalq elmi jurnal, Bakı, cild 2, № 1, 2023, s.54-56.
8. Babayeva S.F. Bakı şəhərində uşaqlarda mono və mikst-rotaviruslu bağırsaq infeksiyası // Ümummilli lider Heydər Əliyevin 100 illiyinə həsr olunmuş «Tibbi profilaktikanın aktual problemləri aktual problemləri» mövzusunda Beynəlxalq elmi-praktik konfransının məcmuəsi, Bakı, 27 oktyabr 2023, s.116-117
9. Rustamova L.I., Kuliyeva Z.M., Qilindjova F.V., Israfilbekova O.B., Isayeva M.M., Mammadova N.O., Babayeva S.F. Features of the epidemic prosess of mixed viral intestinal infection in children in Baku // International Eastern European scientific journal, 2024, part 1, 01(98), p.16-20.
10. Rustamova L.I., Kuliyeva Z.M., Mammadova N.O., Heydarova F.H., M.M.Isayeva, Manafov P.Q., Babayeva S.F.Monitoring the circulation of some serotypes of non-polioenteroviruses in the environment // International scientific journal "Science and education modern time", 2024, vol.2, p.41-47.
11. S.F.Babayeva Epidemiologial characteristics of norovirus intestinal infection among children in Baku city// New day in medicine 2024,10(72), (Taskent) p. 255-260.
12. S.F.Babayeva Bakı şəhərində uşaqlar arasında norovirus infeksiyasının epidemioloji xüsusiyyətləri// Azərbaycan Tibb jurnalı, 2024, №3 s.92-97.

ABBREVATIONS

AstV – Astrovirus
AstV AG – Astrovirus Antigen
AdV – Adenovirus

AdV AG – Adenovirus Antigen
EV AG – Enterovirus Antigen
AII – Acute intestinal infections
AG – Acute gastroenteritis
IIUE – Intestinal infection of unknown etiology
NV – Norovirus
NV AG – Norovirus Antigen
PCR – Polymerase Chain Reaction
RV AG – Rotavirus Antigen
RNA – Ribonucleic Acid
WHO – World Health Organization
HAstV – Human Astrovirus
ELISA – Immunoenzymatic Assay

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