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Review Article

Viral Gastroenteritis Prevalence in Iranian Pediatric Population: A Systematic Review

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Abstract

Background: Viral gastroenteritis infection, a prevalent condition in adolescents and children, is still a rigid and serious problem among humans. This disease is responsible for up to three million fatalities nationwide. noroviruses, rotaviruses, astroviruses, adenoviruses, and sapoviruses are the most common and well-known pathogens associated with viral gastroenteritis agents. In this systematic review, we extracted all original articles and data on viral gastroenteritis that were performed on the Iranian pediatric population.

Methods: To investigate the viral agent pathogens of gastroenteritis in Iran, 48 articles on the identification of viral gastroenteritis were gathered from the existing data. Viral gastroenteritis was detected in fourteen provinces, including the southern and northern parts of Iran. The seasonal distribution in Iran was analyzed as well. Finally, all the data from 1978-2021, along with their detailed information, were summarized, including the number of patients, the number of positive cases, applied technics, and the region of the studied cases in Iran.

Results: Based on the results, most of the viral detection was associated with Rotavirus, the major pathogen responsible for gastroenteritis disease, followed by Adenovirus, Norovirus, Parechovirus, Bocavirus, Astrovirus, Aichivirus, Sapovirus, and three case reports of SARS-CoV-2 that were associated with viral gastroenteritis.

Conclusion: Different studies conducted over Iran, including the northern, southern, and central regions, were obtained based on the data. Most studies had been merely dedicated to rotavirus, which had the highest prevalence of all other viral gastroenteritis. Our review clearly demonstrated that Rotavirus genotype G1P [8] is the dominating sereotype among the other studied gastroenteritis viral agents in Iran in which the most frequency rate was during the winter (44.26%), while the least frequency rate was observed during summer (8.96%).

Keywords: Iranian child gastroenteritis, Viral gastroenteritis, Rotavirus, Adenovirus, Norovirus

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Introduction

Viral gastroenteritis infection has been recognized as a common illness among children and adolescents. Considering that the oral route is regularly the underlying region of the pathogen's exposure, this infection is mainly observed in young children under the age of five and infants. Gastroenteritis infection outbreak happens more often in developing countries where children have no sufficient access to clean water and environmental sanitization (1,2). Studies have shown that the rate of mortality is higher in developing countries; however, the rate of infection cannot be ignored in developed countries either (3). Although gastroenteritis is normally a self-limited disease, it is reported that it accounts for up to three million deaths globally (4,5). Therefore, the investigation of this matter is highly imperative. Due to gastroenteritis symptoms, this disease is also known as infectious diarrhea (2). The symptoms are typically diarrhea, vomiting, fever, and abdominal pain. In acute gastroenteritis, it is possible to observe high dehydration and electrolyte imbalance which can lead to death and hospitalization (6,7).

In today's world viruses are the initial pathogens that are responsible for 75%-90% of infectious diarrhea, and several viruses are involved in this disease (8). Although the discovery of gastrointestinal viruses is still an ongoing project for scientists, noroviruses, rotaviruses, astroviruses, adenoviruses, and sapoviruses are the main and well-known pathogens related to viral gastroenteritis agents (9). The recent coronavirus (coronavirus disease 19, COVID-19) has also been reported for some gastroenteritis symptoms, especially in young children, with the observation of diarrhea and vomiting throughout the phase of illness (10), and the continuous observation of viral RNA positivity in children's stool samples is boosting great concerns regarding the control and inhibition of COVID-19. Human Bocavirus, Aichivirus, and human parechoviruses have also been reported as viral gastroenteritis agents (11).

As mentioned above, the prevalence of acute gastroenteritis in developing countries is higher in comparison with developed countries; therefore, it was aimed to provide a systematic review to make a broader view of this subject in the pediatric population of Iran.

Materials and Methods

Search Strategy and Selection Criteria

The present study was accompanied using the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) checklist (12).

At the beginning of our study, PubMed, Medline, Google Scholar, and National databases were searched through August and September 2021. All of our searches included English and Persian languages without any date restriction. All the databases were searched using keywords and terms such as Acute Gastroenteritis, Viral Gastroenteritis, Child Gastroenteritis, acute Gastroenteritis 'AND' Iran, Viral Gastroenteritis 'AND' Norovirus, Viral Gastroenteritis 'AND' Rotavirus, Viral Gastroenteritis 'AND' Sapovirus Viral Gastroenteritis and Adenovirus, and Viral Gastroenteritis 'AND' Coronavirus. The other keywords were Viral Gastroenteritis 'AND' SAR-CoV-2' Viral Gastroenteritis 'AND' Bocavirus, Viral Gastroenteritis AND Astrovirus, Viral Gastroenteritis AND Aichivirus, Viral Gastroenteritis 'AND Iran, Rotavirus 'AND' Iran Norovirus 'AND' Iran Sapovirus 'AND' Iran Coronavirus 'AND' Iran, Adenovirus 'AND' Iran, and Bocavirus 'AND' Iran, In addition, the reference sections of the studies were reviewed and rechecked to consolidate and identify further relevant studies. Then, the applicable publications which were most relevant to epidemiological and clinical child viral gastroenteritis were selected through our collected data.

Screening and Data Extraction

First, all the publications were studied and screened based on their title and abstracts. The eligible abstracts were selected for the full-text version study. Then, the studies were selected whether they met the inclusion criteria; they included the detection of the viruses (Norovirus, Sapovirus, Rotavirus, Astrovirus, Adenovirus, Coronavirus, Bocavirus, and Aichivirus) in the stool samples of children with acute gastroenteritis, epidemiology of each mentioned virus, the prevalence of each viral infection in children among different cities in Iran, use of reported standardized laboratory techniques for viral detection. On the other hand, studies were excluded if they were applied to species other than human and environmental experiments. All the studies were determined based on their full text, and those which did not meet our criteria were excluded from further investigations. The flow of information in the systematic review is shown in Figure 1. Subsequently, data and information were extracted based on the detection rate of the mentioned viruses in Iranian pediatric patients.

Results

Viral Gastroenteritis Aspects

In this study, 48 articles related to viral gastroenteritis detection were extracted, which were performed on the Iranian population, 3 of which were case reports related to SARS-CoV-2. The features of main viruses associated with viral gastroenteritis among virologic characteristics and patterns are described in Table 1.

All the patients that were recognized with gastroenteritis symptoms were gathered, and then positive cases with various virus detection were divided to bring a wider insight into the study of this disease. The numerical distribution of positive viral gastroenteritis cases among the studied population is illustrated in Figure 2. All the numbers of patients involved in gastroenteritis studies in the Iranian pediatric population from 1987 to 2021 are gathered in this diagram. A total of 17789 patients were diagnosed to have acute gastroenteritis based on their clinical symptoms, approximately all of the patients had diarrhea, and other manifested clinical symptoms included vomiting, abdominal pain, fever, and in some cases, dehydration. Based on the diagram, the number of patients who were involved with Rotavirus was significantly higher compared to other viral agents. It should be noted that studies and investigations of other viral agents were not sufficient to have an accurate overview. There was an investigation over fourteen provinces, along with the northern and southern regions of Iran. Rotavirus, Adenovirus, Aichivirus, Astrovirus, Bocavirus, Sapovirus, and Norovirus were observed in children's stool samples. Three case reports related to SARS-CoV-2 with gastroenteritis symptoms were observed and reported as well. Overall, 5900 positive cases were found to report Rotavirus. Co-infection between Rotavirus and Norovirus was reported in three cases. Except for three case reports related to SARS-CoV-2, the least detection of the viral agent was associated with Sapovirus (eight positive cases). Table 2 presents all the complication reports among viral gastroenteritis cases with the method, frequency, and genotyping if available.

Gastroenteritis was spread widely throughout the year with the most frequency rate during the winter (44.26%), followed by autumn (32.61%), spring (14.19%), and summer (8.96%), which is consistent with the result of other studies in different countries. Figure 3 depicts the spreading points of viral gastroenteritis in geographical

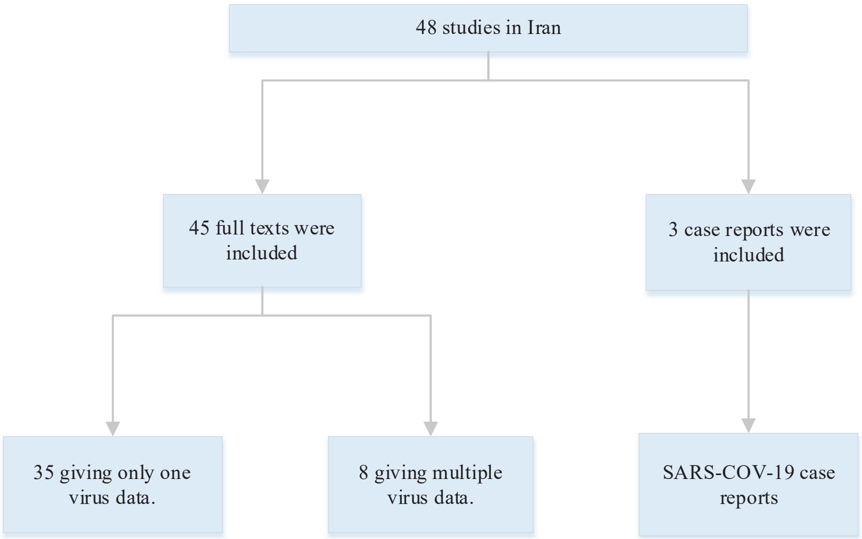

Figure 1. Information Flow Through the Phase of the Systematic Review. Our search was performed using the key words Iran and viral gastroenteritis. Overall, 48 studies were published between 1987 and 2021, including case reports

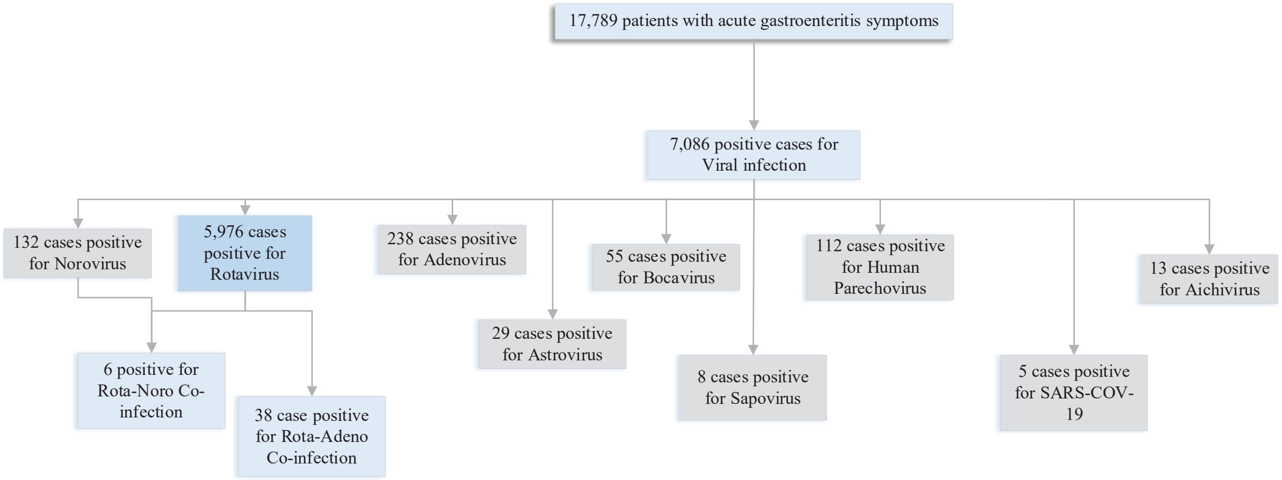

Figure 2. Numerical Distribution of All Viral Gastroenteritis Studied in Iran

Table 1. Virologic Attributes and Means of Main Viruses Associated With Viral Gastroenteritis (13)

Virus	Family	Size (nm)	Genome Size (kb)	Appearance Using EM	Nucleic Acid	Detection Methods
Norovirus (14)	*Caliciviridae*	27-30	7.5	Small, round-structured	Positive-single stranded RNA viruses	RT-PCR, ELISA, & EM
Rotavirus (15)	Reoviridae	70	18.5	Wheel-shaped triple-layered capsid	dsRNA	EM, ELISA, & RT-PCR
Astrovirus (16)	Astroviridae	27-34	6.8-7.9	SRV- star shaped	ss(+)RNA	EM, ELISA, & RT-PCR
Adenovirus (17)	Adenoviridae	70-100	26-45	Icosahedral capsid	dsDNA	EM, EIA, RT-PCR, & culture
Bocavirus (18)	Parvoviridae	20	4-6	Icosahedral and non-enveloped	Single- Stranded DNA	PCR
Aichivirus (19)	*Picornaviridae*	30	8.2	Icosahedral morphology	ss(+) RNA	N-PCR & RT-PCR
Sapovirus (20)	Caliciviridae	30-38	7.4	Cup shaped	Non enveloped ss(+) RNA	EM, ELISA, & RT-PCR
Parechovirus (21)	Picornavirus	30 nm	7.3	Spherical and round geometries	Ss(+) RNA	EM & RT-PCR
Coronavirus (22)	Coronaviridae	60-200	26.4-31.7	Pleomorphic with club-shaped projections	ss(+) RNA	EM & RT-PCR

Note. EM: Electron microscopy; SRV: Standard recovery vehicle; Reverse transcriptase polymerase chain reaction; ELISA: Enzyme-linked immunosorbent assay; EIA: enzyme immune assay.

regions of Iran (a) and its seasonal distribution (b). Further details of the studies that have been conducted in Iran are described in this section.

Norovirus

Farsi et al studied children under 5 years old with acute gastroenteritis and found 36 positive samples for

Table 2. Studies Performed in Iran Related to Viral Gastroenteritis

First Author (References)	Geographical Region and Frequency of Gastroenteritis	Viral Agent Occurrence (%)	Test Method	Genotyping	Gender
Tariverdi (23)	Tehran	SARS-CoV-2 (1 patient)	RT-PCR	NA	Female
Moradveisi (24)	Sanandaj	SARS-CoV-2 (1 patient)	RT-PCR	NA	Female
Ekbatani (25)	Tehran	SARS-CoV-2 (3 patients)	RT-PCR	NA	66.6% Male 33.3% Female
Taghinejad (26)	Karaj, Tehran	Aichivirus (8.1)	RT-PCR	NR	30% Male 70% Female
Farsi (27)	Tehran	Rotavirus (17.1)	RT-PCR	GII 17.1%	56.7% Male 43.3% Female
Shams (28)	Qom	Rotavirus (16.9)	RT-PCR	G1 27% G9 18% G2 9% G3 9% G4 9% G12 5% G non-typable 23% P[8] 50% P[6] 23% P[4] 14% P non-typable 13%	60% Male 40% Female
Farahmand (29)	Tehran	Rotavirus (100)	RT-PCR	P[8] 94.4% P[4] 2.8% P[6] 2.8%	NR
Arashkia (30)	Tehran	HAdV (4.3)	PCR	(AdV41) 62.5% (AdV1,2,6,) 31.25% (AdV3) 6.25%	56.7% Male 43.3% Female
Lorestani (31)	Gorgan, Golestan	Rotavirus (11.17)	Latex agglutination PAGE (Semi-nested multiplex RT-PCR for G and P genotyping)	G1 57% G2 18.70% G3 4.69% G4 3.13% G9 6.26% non-typable 6.26% P[8] 97.80% P[4] 2.20%	61% Male 39% Female
Azaran (32, 33)	Ahvaz, Khuzestan	Rotavirus (32)	Latex agglutination RT-PCR	G9 37.5% G2 21.9% G1 12.5% G12 9.4% G4 9.4% G2G9 6.9% G3 3.1% P[8] 62.5% P[4] 31.5% P[4]P[8] 3.1%	55% Male 45% Female
Mousavi Nasab (34)	Tehran	HAdV (5) HAstV (6.7) SaV (2.5)	RT-PCR	NR	18.2% Male 9.3% Female
Mousavi Nasab (35)	Tehran	Rotavirus (23.3)	RT-PCR	G1 75% G2 14.3% G9 7.14% Mixed G1/G2 3.58% P[8] 75% P[4] 25%	NR
Mousavi Nasab (36)	Tehran	Rotavirus (28.8) Norovirus (8.8) Rota-Noro Coinfection (3.5)	RT-PCR	Norovirus: GII 86.7% GI 13.3% GIV 0%	54.1% Male 45.9% Female
Sharifi-Rad (37)	Zabol	Rotavirus (70.2) Adenovirus (20.3) Norovirus (9.5)	Immunochromatography Test	NR	NR
Azaran (32)	Ahvaz, Khuzestan	Rotavirus (36.5)	ELISA RT-PCR	G and P 86.3% 13.7% non-typable	61.6% Male 38.4% Female
Monavari (38)	Tehran	HBoV (8)	RT-PCR	NR	72% Male 28% Female
Kargar (39)	Yasuj	Rotavirus (28.2)	RT-PCR	G1 1.92% G2 7.69% G4 1.92% G8 46.16% non-typeable 40.39% Mixed 1.92%	12.5% Male 15.76% Female
Khoshdel (40)	Shahrekord	Rotavirus (30)	RT-PCR	G1 20% G9 20% G1G9 13.3% G1G4 6.7% G1G3 3.3% G1G8 3.3.%	53% Male 47% Female
Jadali (41)	Bandar Abbas Shiraz Mashhad Tabriz Tehran	Rotavirus (16.7) (14.2) (7.76) (7.56) (8.97)	ELISA	NR	59.9% Male 40.1% Female
Shokrollahi (42)	Tehran	Rotavirus (48) adenovirus (20) HBoV (20) HPeV (23.2) Adeno-Rota co infection (6)	"Rota and adeno: rapid chromatographic tests HBoV: RT-PCR HPeV-1 : nested-RT PCR"	NR	58% Male 42% Female
Kargar (43)	Borazjan	Rotavirus (27.85)	ELISA Nested Multiplex PCR	G1 52.27% non-typable 40.91% G9 4.54% G4 2.27%	28.4% Male 21.77% Female
Najafi (44)	Borazjan	Rotavirus (24.27) Norovirus (12.35) Adenovirus (5.1) Astrovirus (2.4)	ELISA	NR	NR
Motamedifar (45)	Shiraz	Rota (42) Adeno (9) Rota-Adeno Coinfection (4)	ELISA	NR	59.5% Male 40.5% Female
Romani (46)	Tehran	HBoV (9.18)	PCR	(HBoV1)11.1% (HBoV2) 35.1% (HBov3) 3.7%	48% Male 52% Female
Romani (47)	Tehran	Sapovirus (11.9)	RT-PCR	NR	60% Male 40% Female
Rezaei (48)	Tehran	Adenovirus (8)	PCR	Adv 40 ,41	62.5% Male 37.5% Female
Hamedi (49)	Mashhad	Adenovirus (2)	Lattex Agglutination	NR	NR

Table 2. Continued.

First Author (References)	Geographical Region and Frequency of Gastroenteritis	Viral Agent Occurrence (%)	Test Method	Genotyping	Gender
Romani (50)	Tehran	Norovirus (9.8)	RT-PCR	Noro I 35% Noro II 65%	57% Male 43% Female
Ataei-Pirkooh (51)	Tehran	Rotavirus (43)	Latex agglutination Electron microscopy	NR	NR
Ghazi (52)	Tehran	HPeVs (23.7)	RT-PCR	(HPeV-1)23.7%	35.3% Male 16.0% Female
Ghorashi (53)	Tabriz	Rotavirus (55.6)	ELISA	NR	60.2% Male 39.8% Female
Nadji (54)	Tehran	hBoV (12.8)	PCR	NR	40.4% Male 59.6% Female
Esteghamati (55)	Tabriz Mashhad Northern Region Shiraz Bandar Abbas Southern Region Tehran	Rotavirus (49) (49.4) (66.3) (63.3) (65) (44)	RT-PCR	G4 44.5% G non-typable 36.4% P[8] 64.5% P[4] 6.4% P[9] 0.9% P non-typable 28.2%	NR
Emamghorashi (56)	Jahrom	Rotavirus (67.6)	ELISA latex agglutination test	NR	52.1% Male 47.8% Female
Sadeghian (57)	Mashhad	Rotavirus (28.8)	Latex agglutination test	NR	30.1% Male 27.4% Female
Nakhaei Sistani (58)	Tehran	Adenovirus (6.3)	PCR PAGE	Adv 40 ,41	40%Male 60%Female
Hamkar (59)	Mazandaran	Rotavirus (62) Astrovirus (3) Adenovirus (2.3)	ELISA	NR	64% Male 58.5% Female
Modaress (60)	Tehran	Rotavirus (19)	PAGE RT-PCR	G1 76.3% G4 11.5% G8 0.8% Mixed types 3.1% P[8] 66.4% p[4] 9.2%	NR
Barari Savadkoohi (61)	Babol	Rotavirus (61.6) Adenovirus (2.9) Astrovirus (2.4)	ELISA	NR	61.5% Male 38.5% Female
Farahtaj (62)	Tehran	Rotavirus (24.6)	ELISA RT-PCR	G1 G2 G4 G9 G12 P[4] P[8] P[10]	NR
Modarres (63)	Tehran	Rotavirus (32.3)	ELISA	NR	NR
Kazemi (64)	Isfahan	Rotavirus (30.8)	ELISA	NR	52% Male 48% Female
Zarnani (65)	Tehran	Rotavirus (15.3)	ELISA	NR	62.2% Male 37.7% Female
Khalili (66)	Shahrekord	Rotavirus (72.6)	RT-PCR	combination reported	Only male
Samarbafzadeh (67)	Ahwaz, Khuzestan	Rotavirus (29.5)	PAGE	NR	NR
Saderi (68)	Tehran	Adenovirus (8.7)	MEIA	(AdV40) 3.3% (AdV41) 3.4%	60.1% Male 39.9% Female
Amini (69)	Tehran	Rotavirus (25)	Latex agglutination	NR	26% Male 24% Female

Note. RT-PCR: Reverse transcriptase polymerase chain reaction; ELISA: Enzyme-linked immunosorbent assay; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2; NR, not reported; NA, not available; HBoV, human bocavirus; HPeV human parechovirus.

Norovirus genotype II from children stool's samples out of a total of 210 samples (27).

Mousavi Nasab et al investigated over 170 patients presenting gastroenteritis symptoms and detected 15 Norovirus positive cases (8.8%). They also observed Rota-Noro co-infection which was 3.5%, including 6 samples. In their study, genotyping for Norovirus was also performed on the prevalence of GI (13.3%) and GII (86.7%), and there was no GIV (36). In a cross-sectional study by Najafi et al, the rate of Norovirus was 47 (12.35%) among 375 patients (44). Likewise, Romani et al detected 26 positive samples from a total of 293 (9.8%). Genotyping was performed and 9 (35%) and 17 (65%) samples were found to belong to GI and GII strains, respectively (50).

Rotavirus

In a study by Shams et al, 22 out of 130 Rotavirus were found, and genotyping was conducted for 22 positive samples (for VP7 isolates). G1 was the most predominant sereotype accounting for 27%, no G8 strains were observed, and 23% of samples were non-typable. For VP4 genotyping, P [8] was the most predominant sereotype accounting for 50%, and 13% of the samples were P nontypables among G-P combinations, and G1P [8] 32% was the most frequent genotype (28). Farahmand et al found 108 positive cases out of 108 samples (100%). They evaluated the genetic pattern of VP8 protein from different P genotypes, and the phylogenetic tree showed that all P genotypes related to the Iranian population belonged to P(II) Geno groups, and the most prevalent among them was P [8] accounting for 94.4%, which was a significant result (29). In Gorgan, Lorestani et al conducted a study on children with gastroenteritis, and Rotavirus was detected in 46 out of 349 positive samples for Rotavirus genotype A. They also identified G and P genotypes in positive samples that G1 as the most predominant sereotype among G types

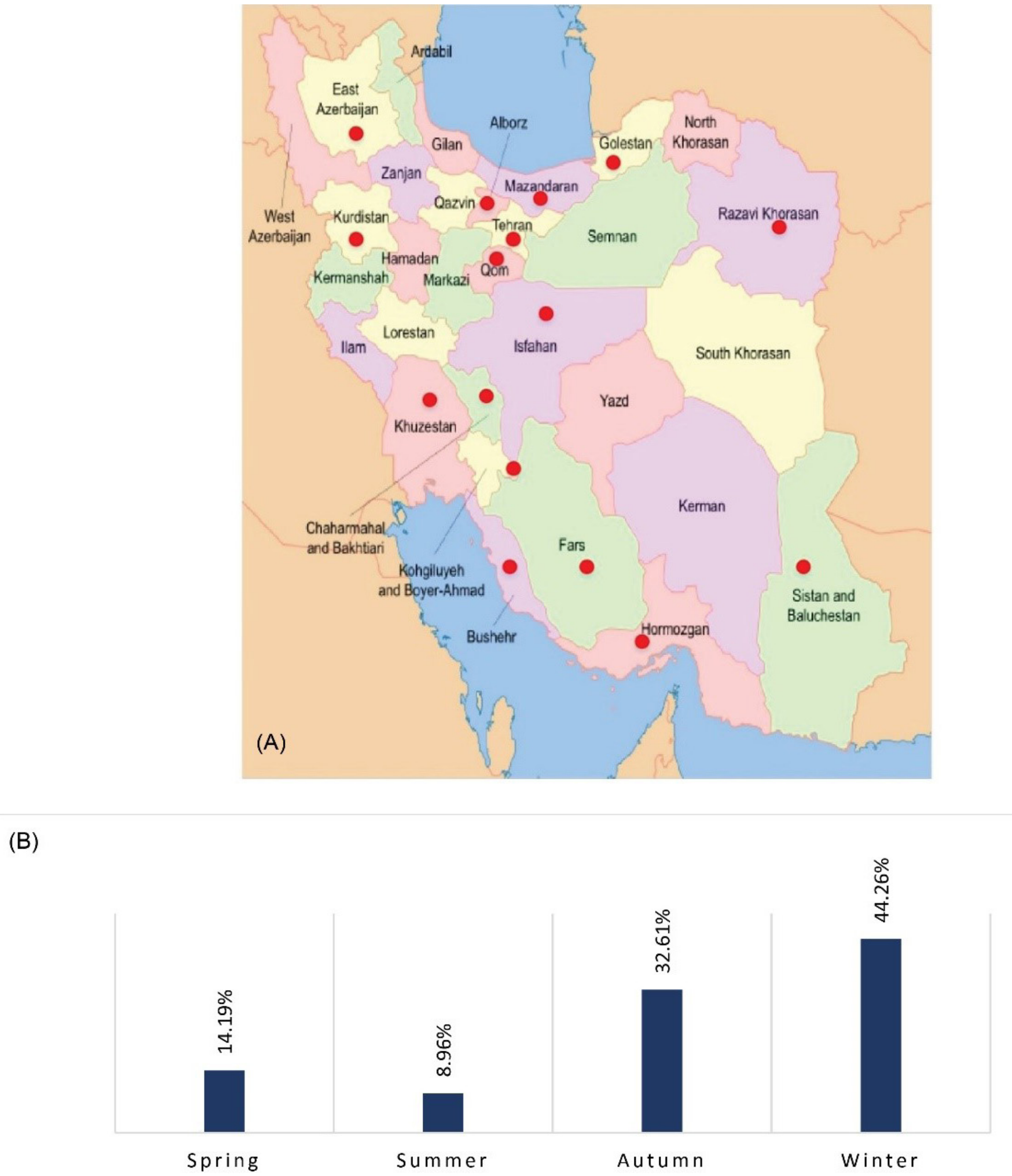

Figure 3. (A) Viral Distribution of AGE in Different Geographical Regions. (B) Seasonal Distribution in Iran 1987-2021

[8]. The predominant G1P [8] 57.82% was the highest rate in G/P combinations in their study as well (31). Similarly, Azaran et al detected 32 positive Rotavirus among 100 stool samples in Ahvaz, Khuzestan. G and P genotyping was performed on positive cases, and G9 turned out to be the most predominant for VP7 genotyping accounting for 37.5%, and VP4 genotyping P [8] with 62.45% was the most common. Among G-P combinations G9P [8] accounting for 28.13% had the highest rate of infection, followed by G2P [4] at 18.75% (33). In another study, Mousavi Nasab et al detected 28 Rotavirus positive out of 130 stool samples, G1 and P [8], accounting for 75% and 75%, respectively, were the most predominant sereotypes (35).

Azaran et al found 73/200 positive for Rotavirus, reporting that G1 (55.6%) and P [8] (83.3%) were the dominant sereotypes in this study (32). Another research in Yasuj during 2010-2011 was performed on Rotavirus genotyping out of 52 positive samples, and G8 was the most common circulating genotype accounting for (46.16%). In addition, the prevalence of the G1 sereotype, which was the most predominant one in the latest research, was only 1.92% (39). Khoshdel et al showed that from 30% positive Rotavirus cases, all under the age of five, G1 and G9 with a prevalence of 20% were the most common ones, mixed genotypes (G1 + G9) (40).

Jadali et al detected 1649 positive Rotavirus from 2988 stool samples; their study was conducted in 5 different cities with the most prevalence in Bandar Abbas (41). In a cross-sectional study by Shokrolahi et al, the prevalence of the Rotavirus in Tehran was 48% (42). In another study by Karegar et al, the prevalence of Rotavirus was 27.85%, and G1 was the most predominant circulating G genotype with a significant percentage of 52.27% (43). In a similar cross-sectional study by Najafi et al, the rate of Rotavirus was 24.27% among 375 patients in Borazjan (44).

Motamedifar et al also conducted a study in Shiraz and reported that 347/827 patients were infected with Rotavirus, which accounted for 42% of the total patients (45). Ataei-Pirkooh et al detected 43 positive Rotavirus among 100 patients with diarrhea (51). Ghorashi et al also found 284 positive cases in a total of 511 stool samples (53). Likewise, Esteghamati et al detected Rotavirus in 5 different cities (Tabriz, Mashhad, Shiraz, Bandar Abbas, and Tehran) plus northern and southern regions among 2198 patients in total. The average percentage of Rotavirus among the mentioned locations was 59.1%. Genotyping for G (VP7) and P (VP4) was performed for 110 samples. G4 (44.5%) and P [8] (64.6%) were the most common among G and P sereotypes, respectively. Among G-P combinations, G4P [8] manifesting at 30.9% was the most predominant strain, and G1P [8] was found at 10.9%. Further, the least combinations were observed among G2P [4] at 5.5%. Moreover, P [8] strains were detected with G non-typeable (21.8%) and G4 with P non-typeable (55).

Additionally, Emamghorashi et al studied 102 patients, and 69 of them (67.6%) were positive for Rotavirus (56). Sadeghian et al also investigated over 156 stool samples of patients in Mashhad among them, 45 samples were positive for Rotavirus (57). In their study, Hamkar et al evaluated 400 patients with diarrhea in Mashhad and detected three different viruses (Rotavirus, Adenovirus, and Astrovirus), and 248 of them were diagnosed to be positive for Rotavirus (59). Furthermore, Modaress et al detected 131 out of 700 stool samples in Tehran; the determination of G and P genotyping showed that G1 (76.3%) was the most common among VP4 genotyping, and P [8] was the most prevalent with the percentage of 66.4% among VP7 genotypes. Finally, G1P [8] turned out to be the highest G-P combination (53.4%) in the detected samples (60).

In a study conducted in one main children's hospital in Amirkola, Babol North of Iran, Barari Savadkoohi et al analyzed 208 samples for the detection of three viral agents (Rotavirus, Adenovirus, and Astrovirus), and the prevalence of Rotavirus was 61.6% among 127 total samples (61). Farahtaj et al also detected 92 positive Rotavirus among 374 patients (24. 6%); in their report, G1P [8] and G9P [8] with a prevalence of 59.2% and 15.5%, respectively, were the predominant genotype combinations (62).

Similarly, Modaress et al detected 404 among 1250 (32.3%). In their study, 341/404 were yielded for electrophoretic patterns. Based on their results, 90% and 8.8% of the strains belonged to long electrophoretic and short electrophoretic patterns, respectively (63). Kazemi et al also detected 57 out of 185 patients with gastroenteritis (64). Likewise, Zarnani et al detected 108 (15.3%) out of 704 patients (65). Khalili et al also detected 146 out of 186 stool samples. It is worth mentioning that in their study, Coronavirus was the second viral agent that was recognized through their research. electrophoretypes were performed for 46 Rotavirus positive samples, and G2P [4] belonged to all short electrophoretype strains, while G1 [P8] and G2P [8] were related to long electrophoretypes (66). In their study, Samarbafzadeh et al found 59 out of 200 samples (67). In another study, Amini et al investigated 229 (25%) positive Rotavirus samples out of 915 patients under 5 years with AGE symptoms in seven hospitals in Tehran (69).

Human Astrovirus

Astrovirus was observed in eight out of 120 patients in a study conducted by Mousavi Nasab et al with a prevalence of 6.7% (32,33). Najafi et al detected 2.4% in nine out of 375 patients (44). Hamkar et al reported Astrovirus among 12 out of 400 patients. The prevalence of this viral agent turned out to be 3% (59). In another study, Barari Savadkoohi et al detected only 5 positive samples out of 208 patients (61).

Human Adenovirus

Based on our investigation, ten studies were found regarding Adenovirus. Arashkia et al detected 16 positive samples for Adenovirus among 376 patients. In their research, they reported the genetic characterization of the human adenovirus as well. HAdv-41 was the most common genotype; interestingly, human adenovirus types C and B were observed as well. HAdV-C, which includes types 1, 2, and 6, was detected in 5 samples (31.25%), and HAdV-B, which represents type 3, was observed in 1 (6.25%) sample (30). Mousavi Nasab et al observed 120 stool samples from children for three viral agents HAdv, Human Sapovirus, and HAstV, among them, 6 positive samples (5%) were found to be positive for Adenovirus (34). In a cross-sectional study by Shokrolahi et al, the rate of Adenovirus was 20%, which included 16 samples out of 80 in their report, and the co-infection of Rota-Adeno was also reported, including 6% of samples (42).

Najafi et al detected 19 (5.1%) positive Adenovirus samples out of 375 patients (44). Moatmedifar et al also found 76 positive Adenovirus samples out of 827 patients, among them, 34 samples were Rota-Adeno coinfection (45). Likewise, Rezaei et al reported only 8 samples out of 100 patients, all eight samples were positive for AdV40-AdV1 (48). In another study, Hamedi et al observed 4 samples positive for adenovirus among 200 patients with diarrhea (49). In the study by Nakhaei Sistani et al, only 5 samples from a total of 80 samples of children were positive for human adenovirus (58). Similarly, Hamkar et al found 9 positive samples for Adenovirus from a total of 400 stool samples. Moreover, Barari Savadkoohi et al reported 6 positive samples among a total of 208 samples (59). Eventually, Saderi et al found 76 positive samples out of 872 samples (68).

Human Bocavirus

Bocavirus was detected in a total of 200 patient samples, and the prevalence of Bocavirus was observed in 16 (8%) samples (38). Bocavirus infection has been investigated through blood, saliva, feces, urine, sewage, and river water. It was reported that this virus is mainly detected in newborns aged 6-24 months (70). Bocavirus case reports have shown a high rate of co-infections such as adenovirus, norovirus, and rotavirus (71).

Shokrolahi et al found 8 positive samples for Bocavirus out of 80 stool samples (42). Romani et al also detected 27 positive samples from a total of 294 patients. In their study, NP1 (10 samples) products of PCR and NS1 (17 samples) were then performed for direct sequencing. The results revealed that 3 and 13 patients were infected by HBoV-1 and HBoV-2, respectively, and only 1 patient was found with HBoV-3 (46). In another study, Najdi et al detected only 6 positive samples out of 47 total samples (54).

Aichivirus

Taghinejad et al first detected the Aichivirus in Karaj, Alborz in the stool samples of Iranian children patients presenting acute gastroenteritis symptoms, the most common clinical symptoms were diarrhea and fever. In addition, 13 out of 160 samples were positive for this virus. In this study, the co-infection of Aichivirus with other common viruses was not detected (Norovirus, human adenovirus, and rotavirus), but 12 and 11 samples were also positive for Salivirus and Saffold virus, respectively, and in one patient, triple infections were observed with the participation of both Salivirus and Saffold virus. The peak season of this viral agent was observed in winter (26).

Human Sapovirus

Sapovirus was detected in the study by Mousavi Nasab et al. Based on their results, 2.5% of Sapovirus belonged to patients in Tehran (34). Romani et al found five positive Sapoviruses among 42 samples (47).

SARS-CoV-2

Tariverdi et al reported diarrhea as the only demonstration of COVID-19 in a 27-month child with fever and bloody diarrhea, and the patient was diagnosed with COVID-19. Her stool and pharyngeal sample were both positive for SARS-CoV-2 (23). Moradveisi et al also reported a 16-month female patient presenting diarrhea, vomiting, and lethargy, and she tested positive for SARS-CoV-2. It is highly important to note that other symptoms related to coronavirus were absent (24). These studies demonstrate that the presentation of COVID-19 in pediatric patients may be various from the typical clinical symptoms of the infection, specifically in comparison with adults, respiratory involvement, and most probably, diarrhea is the highlighted presentation, and long-term isolation must be considered due to the viral shedding.

Human Parechovirus

Shokrolahi et al detected 19 positive HPeV-1 stool samples among 80 patients (42). In another study by Ghazi et al, 472 samples were detected for HPeV-1, and 112 of them were positive (52).

Discussion

Although the viral agent condition regarding gastroenteritis is well determined in many countries, narrowed and limited available data led us to provide a summary of the current situation and studies that have been performed in our country in order to bring insight into this disease.

Based on our gathered data, studies have been conducted in different regions of Iran, including the northern, southern, and central parts of the country. Rotavirus had the most prevalence among other viral gastroenteritis, and the highest number of studies had been exclusively assigned to rotavirus. Our review vividly represents that Rotavirus genotype G1P [8] is the dominant sereotype although other sereotypes and non-typeable strains were observed as well. Given that this disease has a high prevalence among the Iranian children population, vaccination could be a helpful factor to be taken into consideration. Before the advent of the Rotavirus vaccine, this virus has been the main cause of children's gastroenteritis illness, but after the vaccination in some developed countries such as the USA, the rate of morbidity and acute gastroenteritis demonstrated a significant decline. Right now, two vaccines related to Rotavirus, namely, RotaTeq (RV5) and Rotarix (RV1), are recommended by the World Health Organization for the routine immunization of infants (72). Rotavirus vaccines have been introduced into the national immunization program of 82 countries; it is essential to mention that these vaccines do not cover all the strains of Rotavirus; therefore, further investigations on vaccination and this viral agent are necessary (72).

In Iran, not many experiments and studies have been performed on other viral agents such as human Parechovirus (2 studies), Norovirus (5 studies), Bocavirus (4 studies), Astrovirus (4 studies), Sapovirus (2 studies), and Aichivirus (1 study). Therefore, further investigation over other pathogenic agents associated with other viral gastroenteritis is far essential (73).

The very first record of SARS-CoV-2 associated with the gastrointestinal tract was reported in China (73). Significantly, the detection and proof of SARS-CoV-2 in patient fecal samples have increased great concerns toward COVID-19 disease control (74). In a review article studied by Gupta and his team, it was pointed out that COVID-19 diarrhea has mostly been observed 1-8 days after the disease onset, with a medium period of 3.3 days (10,75). It also has been reported that a number of patients had diarrhea as the initial symptom, and one-third of diarrhea has been watery, and it lasted for 1-14 days (76).

In addition, the viral receptor angiotensin-converting enzyme 2 was found to be expressed in gastrointestinal epithelial cells (77). In one study, 39 out of 73 COVID-19-positive patients (53%) had positive SARS-CoV-2 RNA in their stool samples, and the duration was reported as 1-12 days. What is highly essential in this case is that 17 patients still had positive RNA stool samples after receiving the negative test result from the respiratory tract

(78). In one research, 8 out of 10 children tested positive for rectal swabs regardless of the negative nasopharyngeal tract. Another study verified viral shedding in children with COVID-19 and reported diarrhea in three out of ten infected children (11). The evident continuous updates have provided noteworthy information related to the feasible transmission of COVID-19 through the oral route. Studies suggest that the gastroenteritis tract may shed the virus, and oral-fecal transition might be feasible (79). The majority of public health initiatives to manage and prevent viral gastroenteritis infections have been concentrated on identifying and managing outbreaks (80). Considering that foodborne exposures generate a substantial share of illnesses, efforts have been made to develop techniques for identifying and eradicating virus infection from food sources (81). Furthermore, regular hand washing, avoiding contact with virus-infected individuals, and disinfecting contaminated environmental surfaces are all recommended in this regard (82). It is important to note that gastroenteritis in young children, particularly in infancy, decreased after the rotavirus vaccine was introduced in Taiwan (83). Therefore, more studies on vaccination and the effects of vaccines and different strains of various gastroenteritis agents are needed to have more sufficient control over the illness.

Conclusion

In general, considering that the prevalence of this disease is still high, current data collection indicates that research into viral gastroenteritis agents, and more especially, their nucleic acid genotypes, will have a significant impact on efforts to prevent viral gastroenteritis agents in humans, particularly newborns, children, and vulnerable adults.

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Authors' Contribution

NM contributed for bibliographic review and written paper, MAM guaranteed for statistical and graphic notes, MP and GGJR added for bibliographic review and AM contributed for discussion and final manuscript correction.

Conflict of Interests

The authors declare that they have no conflict of interests.

Ethical Approval

Not applicable.

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