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Review Article

Prevalence of Norovirus in Patients with Acute Gastroenteritis in Iran: A Systematic Review and Meta-Analysis

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Abstract

Background and Aims: Norovirus is the common etiologic agent of acute gastroenteritis. This study aimed to provide a systematic review and meta-analysis of norovirus prevalence in Iranian patients with acute gastroenteritis.

Material and methods: A literature search was done in PubMed (Medline), Web of Science, Embase, Scopus, Google Scholar and Iranian databases (IranMedex, Scientific Information Databank) until December 2023. The keywords were Norovirus, Gastroenteritis, Prevalence, and Iran. The information, including first author's name, Iranian province or city, publication date, study period, sample size, the number of norovirus-positive subjects, laboratory detection method, age groups, gender, and the norovirus genogroups were extracted from articles.

Results: Seventeen articles, involving 4794 patients, were included in the meta-analysis. The pooled prevalence of norovirus was estimated at 9% (95% CI: 6% - 12%). The pooled prevalence of norovirus GI and GII genogroups was 1% (95% CI: 0% - 2%) and 9% (95% CI: 6% - 14%), respectively.

Conclusions: To manage norovirus-related gastroenteritis, monitoring patients with acute gastroenteritis is essential.

Keywords: Norovirus, Gastroenteritis, Prevalence, Iran

Introduction

Acute gastroenteritis (AGE) is a major cause of morbidity and mortality in children worldwide. Etiologic agents of the AGE include bacteria, fungi, parasites, and viruses. Among the viruses causing AGE in children are Rotaviruses, enteric Adenoviruses, Noroviruses, Sapoviruses, Parechoviruses, Aichiviruses, Picobirnaviruses, Toroviruses and Coronaviruses (1-2). Rotaviruses are causative agents of about 40% of the AGE in children, while other viruses account for about 30% (2).

Nowadays after vaccine development for rotavirus, norovirus has an important role in AGE in children. Norovirus causes moderate to severe AGE similar to rotaviruses in children (3). Norovirus is associated with about a fifth of all AGE subjects (4). Norovirus as the major etiologic agent (18%) of sporadic and epidemic cases of AGE in all age groups causes more than 699 million gastroenteritis and approximately 212,000 deaths annually in the world (5). The prevalence of norovirus was deter-

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mined to be 19.04% in the world. The prevalence rate was higher in winter, and differed according to countries and age groups (6).

Noroviruses classified in the *Caliciviridae* family, non-enveloped viruses with a single-stranded (+) RNA genome approximately 7.5 kb in length. VPg protein is covalently attached to the 5'-terminus of the genome, whereas the 3'-terminus is polyadenylated. The viral genome contains three open reading frames (ORFs). ORF1 encodes a polyprotein that, after translation, is processed into viral non-structural proteins responsible for viral replication, ORF2 encodes the major capsid protein (VP1), and ORF3 encodes the minor capsid protein (VP2). Based on the complete VP1 amino acid sequence, noroviruses are classified into ten genogroups (GI - GX) (7). The genogroups GI, GII, and GIV can infect humans while GIII infects bovine species and GV infects mice species (8). According to gene sequencing of viral RNA polymerase and VP1-VP2 junction the genogroups are further subdivided into 49 genotypes (2). For example, GII, the most prevalent genogroup in humans, contains 19 genotypes. The most prevalent genotype is GII.4. According to genetic evolution, noroviruses show at least six mutant strains reported to cause pandemics (5, 8).

Noroviruses are transmitted fecal-oral route, directly from person to person and indirectly through contaminated water and food. They are very contagious and about twenty virions can cause a disease. They are usually prevalent in the winter season. In the world, the prevalence of norovirus in children less than 5 years old, more than 5 years old, and mixed age was the same (16%-19%). Norovirus causes diarrhea, vomiting, fever, headache, and stomach pain. It is accompanied by dehydration and electrolyte loss. Gastroenteritis appears 12 to 48 hours after exposure to the virus, and recovery usually takes 1 to 3 days. There is no antiviral drug treatment for norovirus infection.

Prevention includes washing hands, cleaning, and disinfecting contaminated surfaces. Different genotypes of norovirus may circulate in the world and countries (8).

Severe cases of AGE are common among vulnerable patients including infants, the elderly and immunocompromised patients (9). Longer viral shedding was found among immunocompromised patients (10). Available treatment is limited to supportive care such as rehydration therapies. To date, there is no approved norovirus vaccine; however, several vaccine candidates are currently in development. Due to the substantial economic burden of norovirus AGE, a vaccine could have an important impact to protect AGE in vulnerable patients in the world (9).

Norovirus in stool specimens of patients with gastroenteritis can be detected by using enzyme-linked immunoassay (ELISA) and immunochromatographic assays tracing viral antigens, by reverse transcription polymerase chain reaction (RT-PCR) and real-time RT-PCR for viral RNA, as the gold standard tests for norovirus detection (11).

Farahmand et al, in a meta-analysis review, estimated the prevalence of norovirus in pediatric patients with gastroenteritis worldwide and evaluated the relationship between norovirus and pediatric gastroenteritis. The pooled prevalence of norovirus in children with gastroenteritis was 17.7%. The pooled OR (odd ratio) of the norovirus association with gastroenteritis was 2.7. The most prevalent norovirus genotypes were GII.4 (59.3%) and GII.3 (14.9%). The norovirus was prevalent among the younger age group (less than one year) and males (2).

Farsi M et al evaluated the prevalence and molecular epidemiology of noroviruses in hospitalized children with AGE and age of fewer than five years in Tehran, Iran. The prevalence of the GII norovirus was 17.1% (12). In another study done by Mousavi Nasab SD and et.al, the prevalence of noroviruses was 8.8% in Tehran, Iran. Among the 15 norovirus-positive specimens, 13 (86.6%) were GII, and two (13.3%) were GI (13).

Despite all studies were done on the prevalence of norovirus infection in Iranian patients with AGE. Still, the results were variable and there was not an updated and comprehensive report. The present study was designed to provide a systematic review and meta-analysis of the prevalence of norovirus and its genogroups

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among Iranian patients with AGE based on the articles published between 2010 and 2023.

Methods and Materials

Methods

The present systematic review and meta-analysis were based on the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guideline (14).

Literature Search Strategy

A systematic literature search was done about the prevalence of norovirus infection among Iranian patients with acute gastroenteritis on databases, including PubMed (Medline), Web of Science, Embase, Scopus, Google Scholar and Iranian databases (IranMedex, Scientific Information Databank) until December 2023. The keywords used for article identification were norovirus, gastroenteritis, prevalence, and Iran. All related keywords were selected from the Mesh database. At the end of the literature search, all of the identified articles and their full texts were imported into the EndNote software (version 20, Thomson Reuters), and duplicate articles were removed.

Article Selection and Eligibility Criteria

The articles were screened based on the title, abstract, and full text for selecting eligible articles, considering the inclusion and exclusion criteria. The inclusion criteria were as follows: (1) Original cross-sectional studies (descriptive and analytical) related to the prevalence of norovirus among Iranian patients with acute gastroenteritis published in peer-reviewed journals, despite the language; (2) Studies detecting the norovirus genome in stool specimens by reverse transcription polymerase chain reaction (RT-PCR), nested RT-PCR, and real-time RT-PCR methods; (3) Studies detecting the norovirus antigen in stool specimens by enzyme immunoassay (EIA), rapid immunochromatography; and (4) Studies reporting norovirus genogroups and genotypes in Iran.

The exclusion criteria were as (1) The prevalence of norovirus among Iranian children with underlying conditions; (2) Studies that failed to present data clearly, studies that do not report sample size and frequency of norovirus positive cases or prevalence; (3) Review articles, case studies, conference abstracts, description of diagnostic methods; (4) Studies used other than stool specimens for norovirus detection; (5) Studies reporting seroprevalence of norovirus, (6) Non-human studies, environmental specimens such as food and water; and (7) Studies that had not yet been published and were in the peer-review phase.

Qualitative Assessment

Two reviewers independently conducted the quality assessment of the included studies. According to Damian Hoy's study, the quality of selected articles was assessed by the risk of bias, including external (Items 1 to 4) and internal (Items 6 to 10) validity.

The items were the sampling frame, the sampling methods, the nonresponse bias, the case definition, the data collection, the laboratory technique, and the source of data. If the answer to the question was yes, it would get one point, If the answer was no, it would not get points. In addition, If the answer to the question was unknown it would get 0.5 points. The risk of bias scores from 0 to 5 was classi-fied as high, from 5.5 to 8 as medium and from 8.5 to 10 as low.

Data Extraction

The following data was extracted from the eligible articles, by two investigators independently: first author’s name, name of province or city, publication date, study period, sample size, frequency (prevalence) of norovirus-positive subjects, laboratory detection method, age groups, gender, season of sampling, norovirus genogroups and genotypes.

Statistical analysis

The sample sizes and frequency of norovirus-positive cases among patients with gastroenteritis were extracted from all included studies. Based on the extracted information, Metan and Metaprop commands were used to calculate the cumulative prevalence and the results analyzed. Cochrane Q and I^2 tests were used to evaluate the heterogeneity of selected studies and the variance between them in meta- analysis.

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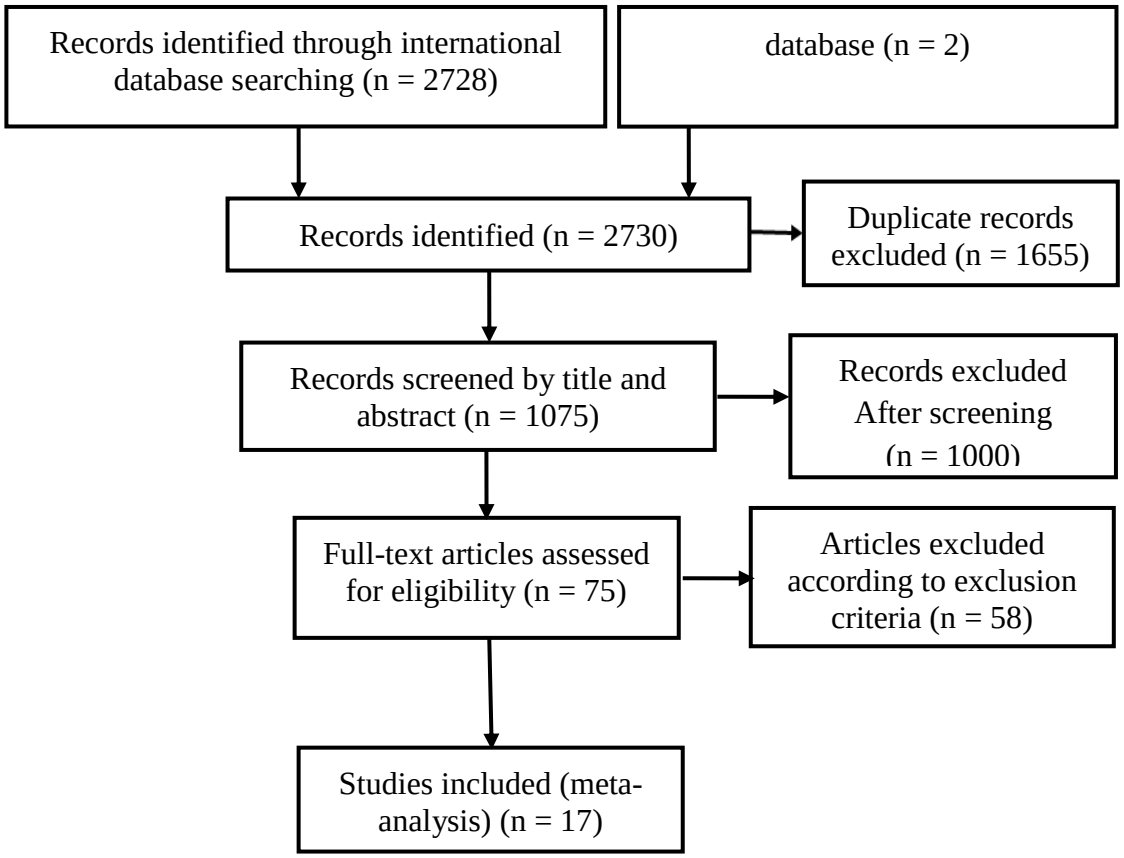

Fig. 1. Study flow diagram

The Egger test was used to evaluate the publication bias. Statistical analysis was conducted using STATA 17.0 and a P-value <0.05 was considered significant. For an analysis of the norovirus infection trend, the study period (years of sampling) of the articles was considered.

Results

Literature Search

According to the preliminary literature search strategies, 2728 studies were identified in databases such as PubMed (Medline), Web of Science, Embase, Scopus, and Google Scholar. Then, two additional articles were identified through Iranian databases (IranMedex, Scientific Information Databank). From the 2730 studies screened, 2655 non-relevant or duplicate articles were excluded after reviewing titles and abstracts. After further assessing the full texts of the remaining article, 58 articles were excluded according to exclusion criteria. Finally, 17 studies (14 in English and three in Persian language journals) were eligible and included in the meta-analysis (Figure 1).

Characteristics of Studies

The study designs of the included articles were cross-sectional. Our review involved 17 studies done in the provinces or cities of Iran as their names appeared in the paper's titles or methods (Table 1).

The articles were published from 2010 to 2023, but the sampling date in the studies was, from 2006 to 2022; two studies did not report the sampling date. The study period ranged from one year to as long as two years in original research. Total sample sizes of 4794 Iranian patients with acute gastroenteritis were included. Acute gastroenteritis was mentioned and defined in the articles. The samples mainly came from Tehran (2071) and Shiraz (690).

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Table 1: Description of 17 studies included in the present study for estimation of the pooled prevalence of norovirus infection in Iranian patients with gastroenteritis

Province or City	Sample Size	Publication Year	Study Period	N (%) of norovirus positive cases	Virus Detection Method	N (%) of norovirus positive cases		The age group of the study population (mean age of norovirus-positive cases)	Season	Setting*	Norovirus Genogroup		Ref
						Male	Female				GI	GII	
Tehran	200	2023	2021-2022	40 (20%)	RT-PCR and Sequencing	NR	NR	less than 5 years	NR	NR	2 (5%)	38 (95%)	(15)
Arak	173	2022	2015-2016	1 (0.57%)	RT-PCR	NR	NR	Less than 7 years	NR	NR		1 (100%)	(16)
Ilam	103	2020	2015-2017	13 (12.8%)	real-time RT-PCR	8 (61.53%)	5 (38.46%)	less than 5 years	Spring	H	2 (15.4%)	11 (84.6%)	(17)
Tehran	211	2019	2015-2016	37 (17.5%)	real-time RT-PCR	23 (62.16%)	14 (37.83%)	less than 5 years (10.9±7.7 months)	NR	H	0	37 (100%)	(7)
Tehran	99	2019	2014-2015	18 (18.2%)	RT-PCR and Electron microscopy	12 (66.7%)	6 (33.3%)	less than 5 years	NR	H	0	18 (18.2%)	(18)
Tehran	210	2018	2015-2016	36 (17.1%)	real-time RT-PCR, Sequencing	23 (63.9)	13 (36.1)	less than 5 years (12 months)	All seasons	H	Not Tested	36 (100%)	(12)
Tehran	170	2016	2013-2014	15 (8.8%)	RT-PCR and Sequencing	10 (66.66%)	5 (33.33%)	less than 5 years (less than 24 months)	Cold seasons	O and I	2 (13.3%)	13 (86.6%)	(13)
Pardis	126	2016	2014	6 (4.76%)	RT-PCR	NR	NR	less than 27 years	NR	O	NR	NR	(19)
Zabol	82	2015	2013	27 (32.9%)	Rapid immunochromatography	15 (55.55%)	12 (44.44%)	less than 1 to 12 months	Winter	O and I	NR	NR	(20)
Iran	2170	2013	NR	90 (4.14%)	RT-PCR	NR	NR	less than 5 years (48 months)	NR	H	NR	NR	(21)
Tehran	570		NR	21 (0.97)		NR	NR		NR		NR	NR	
Tabriz	360		NR	14 (0.64)		NR	NR		NR		NR	NR	
Mashhad	240		NR	4 (0.18)		NR	NR		NR		NR	NR	
Shiraz	690		NR	34 (1.50)		NR	NR		NR		NR	NR	
Bandar Abbas	310		NR	17 (0.78)		NR	NR		NR		NR	NR	
Borazjan	375	2013	2008-2010	47 (12.53%)	ELISA	NR	NR	less than 7 years (12-17 months)	Autumn	H	NR	NR	(22)
Tehran	293	2012	2008-2009	26 (9.8%)	RT-PCR and sequencing	NR	NR	1 month to 85 years (11.72 years)	Summer	H	9 (35%)	17 (65%)	(23)
Ahvaz	143	2012	2008-2009	9 (6.3%)	Nested-RT-PCR	5 (55.55%)	4 (44.44%)	less than 5 years	Winter	H	0	9 (6.3%)	(24)
Tehran	204	2011	2008-2009	23 (11.3 %)	RT-PCR	10 (43.48%)	13 (56.52%)	under 10 years (4±2.8 years)	Autumn	H	6 (26%)	17 (74%)	(25)
Ahvaz	121	2011		1 (0.8%)	RT-PCR	NR	NR	less than 5 years	NR	H			(26)
Tehran	67	2010	2008	3 (4.5%)	RT-PCR	NR	NR	older than 18 years (32±8 years)	Autumn	H	3 (4.5%)	0	(27)
Tehran	47	2010	2006-2008	10 (21.3%)	Nested-RT-PCR and sequencing	6 (60%)	4 (40%)	children up to 17 years (30.26±28.61 years)	Cold seasons	H	0	10 (100%)	(28)

*H: Hospital, O: Outpatient, and I: Inpatients

Most studies reported age groups of patients and laboratory detection methods. Studies' screening tests of norovirus infection based on detecting the viral RNA using RT-PCR and real-time RT-PCR. In some articles, Nested RT-PCR, Sequencing, and Electron microscopy verified the test results. Screening tests of two articles were Rapid Immunochromatography and ELISA for detecting the norovirus antigen in stool specimens. Most studies reported the positive norovirus test in patients, according to age group, gender, the season of sampling, and virus genogroup (GI and GII). Out of 17 articles, the study populations of 12 articles were hospitalized patients (Table 1).

Clinical findings were reported in eight articles including, fever, vomiting (>3 episodes/day), diarrhea (>3 episodes/day), abdominal cramp, respiratory symptoms, malaise, and myalgia. However, we did not analyze clinical data. In addition, the studies were categorized according to virus detection methods, geographic regions, age groups, gender, years of publication and study period (years of sampling) (Table 2).

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Table 2: The prevalence of Norovirus infection in patients with gastroenteritis is categorized based on detection methods, geographic regions, age groups, and years of study.

Variables	No. of Studies	Pooled Prevalence (95% Confidence Interval)	Heterogeneity Assessment	
			I square	P value
Detection methods				
RT-PCR	10	4 % (2 – 5 %)	88.95 %	<0.0001
Rapid	1	33 % (23 – 44 %)	-	-
Immunochromatography	1	13 % (9 – 16 %)	-	-
ELISA	2	9 % (5 – 14 %)	88.90 %	<0.0001
Nested-RT-PCR	3	16 % (12 – 20 %)	-	-
Real-time RT-PCR				
Geographic regions				
Center	10	11 % (7 – 15 %)	90.42 %	<0.0001
West	2	5 % (3 – 8 %)	69.09 %	0.089
East	1	2 % (0 – 4 %)	-	-
South	3	8 % (4 – 14 %)	92.98 %	<0.0001
Age groups				
< 7 years	11	8 % (5 – 11 %)	92.81 %	<0.0001
> 7 years	4	10 % (6 – 15 %)	63.83 %	<0.050
Gender				
Boy	9	9 % (6 – 12 %)	67.33 %	<0.0001
Girl	10	5 % (3 – 8 %)	68.66 %	<0.0001
Year of Publication				
<2015	18	8 % (6 – 10 %)	81.44 %	<0.0001
≥ 2015	4	11 % (2 – 24 %)	89.10 %	<0.0001
Study Period (Years)				
2006 – 2008	6	10 % (7 – 13 %)	81.73 %	<0.0001
2009 – 2011	1	1 % (0 – 5 %)	92.42 %	<0.0001
2012 – 2014	10	7 % (4 – 9 %)	88.00 %	<0.0001
≥ 2015	3	16 % (13 – 20 %)	94.48 %	<0.0001

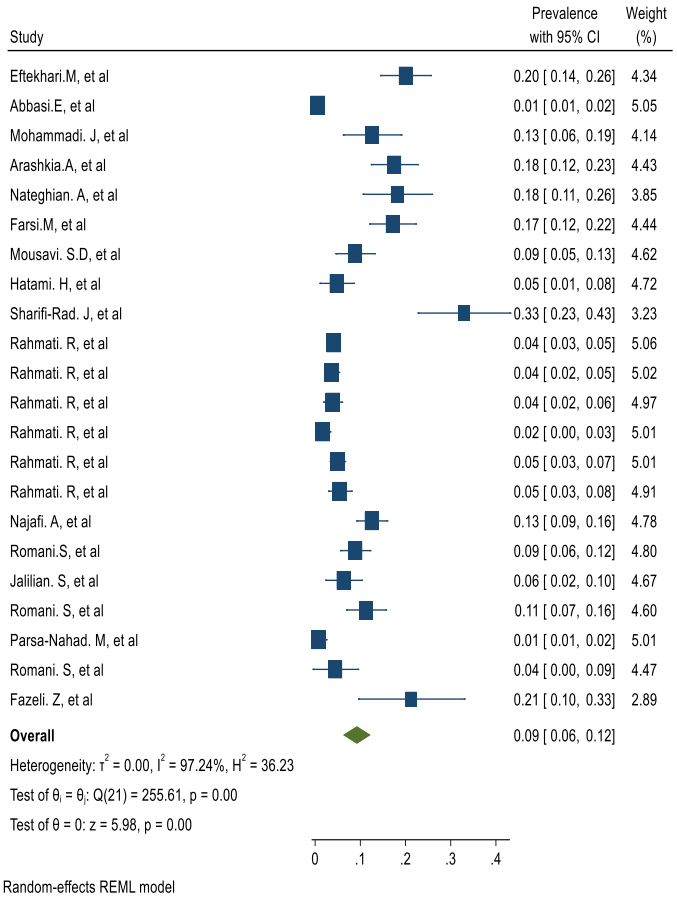

Fig. 2. Forest plot showing the pooled prevalence of norovirus in Iranian patients with acute gastroenteritis. The prevalence of Norovirus is shown on the X-axis and the included articles are shown on the Y-axis. The boxes represent the point prevalence estimate of each study and the horizontal lines represent the 95% confidence interval (CI) of each selected study. The diamond represents cumulative prevalence of Norovirus in Iran and the 95% CI of the.

The Pooled Prevalence of Norovirus

Results of 17 studies with a total sample of 4794 subjects were combined and analyzed; the pooled prevalence of norovirus infection among patients with acute gastroenteritis in provinces and cities of Iran was estimated at 9% (95% CI: 6% -12%), using random effect model. The heterogeneity in this analysis was 97.24%, indicating a significant difference in the methodology and nature of the combined studies (Figure 2).

Egger's test analysis regarding publication bias suggested the presence of bias in this analysis (B: 1.172; SE: 0.463; P value: 0.011). To better evaluate and determine the impact of this bias, Trim and Fill analysis was used, revealing that this bias did not have a significant effect on the calculated cumulative (pooled) prevalence: 0.078; 95% CI: 0.033 – 0.088. The result of the meta-analysis is shown in Figure 3.

Subgroup analyses based on diagnostic methods, geographical regions, age groups, gender, years of publication and study period (years of sampling) were performed. A significant difference in prevalence rates of norovirus infection was observed according to detection methods, geographical regions, age groups, years of publication and study period (p<0.0001). The highest rate of pooled prevalence of norovirus infection was in the Center and South of Iran, 11% (95% CI: 7% - 15%), and 8% (95% CI: 4% - 14%), respectively. The lowest prevalence was in the East of Iran, with a rate of 2% (95% CI: 0% - 4%) (Table 2).

Regarding age groups and years of data collection, the highest prevalence was found in the age group older than 7 years at 10% (6-15%). The results also indicated that the prevalence of Norovirus in boys with gastroenteritis was higher than in girls, with a prevalence of 9% (6-12%) (Table 2).

Among 17 studies included in the present study, seasons were reported in 10 articles, all seasons (two articles), spring (one article), autumn (three articles), winter (two articles), and cold seasons (two articles). However, seven

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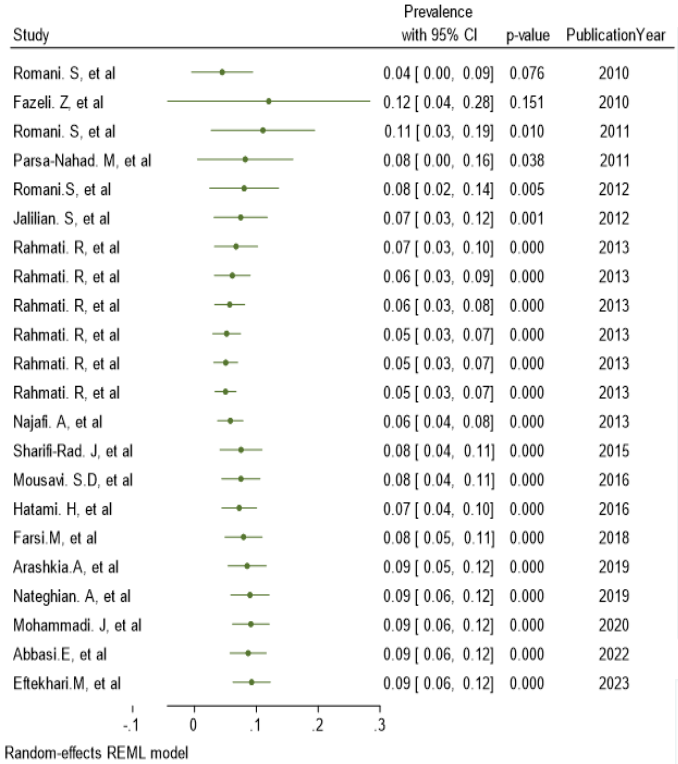

Fig. 3. Cumulative Meta-Analysis and Funnel Plot for Publication Bias in Estimating the Cumulative Prevalence of Norovirus in Patients with Acute Gastroenteritis in Iran.

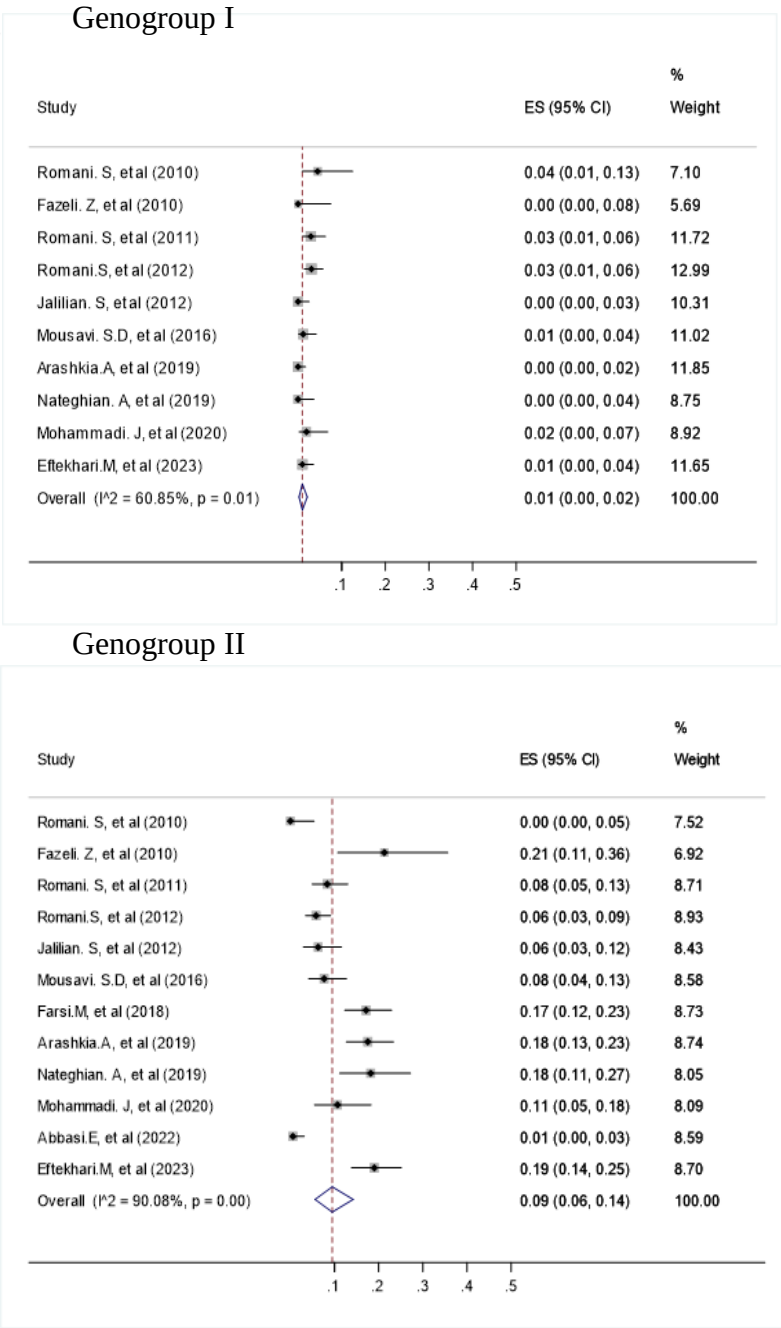

Fig. 4. Forest plot showing the Pooled Prevalence of Norovirus Genogroup I and II in Iranian Patients with Gastroenteritis. ES: effect size

articles did not report the season of sampling (Table 1).

Norovirus infection Trend

All included studies were categorized into four groups according to the year of study. During 2006 – 2008, the norovirus infection prevalence was 10% (95% CI: 7% - 13%). Then, during 2009 – 2011 the prevalence of norovirus infection decreased to 1% (95% CI: 0% – 5%). However, the prevalence rate increased to 7% (95% CI: 4% - 9%) from 2012 to 2014 and 16% (13 – 20%) in 2015 (Table 2).

Norovirus Genogroup

The pooled prevalence of norovirus genogroups GI and GII among Iranian patients with gastroenteritis were 1% (95% CI: 0% - 2%) and 9% (95% CI: 6% - 14%), respectively (Figure 4).

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Discussion

The pooled prevalence of norovirus infection among patients with acute gastroenteritis in provinces and cities of Iran was estimated at 9% (95% CI: 6% - 12%) using the random effect model. The highest rate of pooled prevalence of norovirus infection was in the center and south of Iran, 11% (95% CI: 7% - 15%), and 8% (95% CI: 4% - 14%), respectively. The lowest prevalence was in the East of Iran, with a rate of 2% (95% CI: 0% - 4%). A significant difference in prevalence rates of norovirus infection was observed according to detection methods, geographical regions, age groups, gender, and years of study ($p<0.0001$). The screening tests for norovirus infection often were based on detecting viral RNA using RT-PCR. The pooled prevalence of norovirus Genogroups GI and GII among Iranian patients with gastroenteritis were 1% (95% CI: 0% - 2%) and 9% (95% CI: 6% - 14%), respectively.

The results of this research provide valuable insights into the prevalence of norovirus infection among patients with acute gastroenteritis in different provinces and cities of Iran. The pooled prevalence of norovirus infection was estimated to be 9% with a confidence interval of 6% - 12%. This means that, on average, 9% of the patients with acute gastroenteritis in Iran were infected with norovirus. It's important to note that this estimation was obtained using a random effect model, which takes into account the variation between different studies.

The analysis also revealed significant differences in the prevalence rates of norovirus infection based on several factors. These factors include the detection methods used, geographical regions, age groups, and years of study. This suggests that these factors can influence the likelihood of norovirus infection among patients with acute gastroenteritis.

Among the geographical regions studied, the center of Iran had the highest pooled prevalence of norovirus infection at 11%, followed by the south and west regions with a prevalence rate of 8%. On the other hand, the east region had the lowest prevalence rate at 2%. This indicates that there are regional variations in the prevalence of norovirus infection within Iran.

At least in the temperate area, norovirus is prevalent in winter (29). The data collected from the included studies also provided information on the seasonality of norovirus infection. The majority of studies reported seasonality data, with the highest number of studies reporting data for autumn. However, it is worth noting that some studies did not report the season of sampling, which may introduce some limitations to the analysis of seasonality.

Furthermore, the research examined the trend of norovirus infection over time. The prevalence of norovirus infection was found to be 10% during 2006-2008 but decreased to 1% during 2009-2011. However, there was an increase in prevalence to 7% from 2012-2014. These fluctuations suggest that the prevalence of norovirus infection among patients with acute gastroenteritis in Iran is not consistent and may vary over time.

A systematic review and meta-analysis were done by Farahmand M et al to evaluate norovirus prevalence in pediatric patients with gastroenteritis worldwide from 1 January 2015 to 29 May 2020. A total of 123 articles were included in the analysis. The pooled prevalence of norovirus in 120531 children with gastroenteritis was 17.7% among 45 countries in the world. There were 28 case-control studies, and the pooled prevalence of norovirus in 11,954 controls was 6.7%. The association between norovirus and gastroenteritis was analyzed, and the pooled odds ratio was 2.7. The most prevalent norovirus genotypes were GII.4 (59.3%) and GII.3 (14.9%). The highest frequency of norovirus was found in less than one year of age and males (2).

Liao Y et al in a large area to estimate norovirus prevalence among patients with gastroenteritis worldwide did another systematic review and meta-analysis. Databases were searched for articles that applied PCR to assess the prevalence of norovirus in patients with acute gastroenteritis from 2014 to 2021. In 405 articles with 842926 subjects, the pooled prevalence of norovirus was 16%. Norovirus infection risk was high among children under five years old. A higher prevalence of norovirus infection was

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in South America (22%), and a similar result was seen in other continents. A decreasing trend of norovirus infection prevalence was seen in the community (20%), outpatients (18%), hospital setting (17%), and inpatients (15%) (30).

Another systematic review and meta-analysis reported the prevalence of norovirus infection in Africa. Twenty-one articles were included for the pooled prevalence of norovirus, and out of the 21 articles 11 analyzed the viral strains. Studies have been conducted since 2006, conducted among symptomatic cases including all age groups and detected by using molecular methods. The prevalence of norovirus was estimated at 20.2%. The highest prevalence was in Ghana (36.3%). The prevalence of GII was estimated at 89.5%. The highest and lowest prevalence of GII was 98.3% in Ethiopia and 72.4% in Burkina Faso, respectively. The pooled prevalence of GII.4 was 50.8%, followed by GII.6 (7.7%), GII.17 (5.1%), GI.3 (4.6%) and GII.2 (4.2%) (31).

In another systematic review and meta-analysis databases were searched from Jan 2008 to March 2014, for articles that used PCR-based tests to estimate the prevalence of norovirus in patients with acute gastroenteritis. 175 articles were included; the pooled prevalence of norovirus in 187336 patients was 18%. The prevalence of norovirus was higher in the general population (24%) and outpatients (20%) compared with inpatients (17%). Prevalence was higher in developing (19%) and developed (20%) low-mortality countries compared with high-mortality developing countries (14%, 11-16). There was no association between norovirus prevalence with the patient's age and the studies that were done during the emergency of a novel strain (4).

A systematic review estimated the prevalence of norovirus in patients with gastroenteritis in developing countries based on articles published from January 1, 1990, to March 31, 2016. Articles were included with a study period of at least 12 months and provided information on PCR-tested norovirus infection in patients with acute gastroenteritis. In 178 studies, containing 148,867 subjects with acute gastroenteritis the estimated prevalence of norovirus was 17%. The prevalence was 18% in upper-middle-income countries, but decreased to 15% and 6% in lower-middle countries and low-income countries, respectively. There were no significant differences in norovirus prevalence according to age (≤ 5 years, ≥ 5 years, and mixed ages) or clinical settings (community, outpatients, and inpatients). The pooled prevalence of norovirus GII (15%) was higher than norovirus GI (1%) (32).

In comparison to the results of previous studies conducted in the world, the pooled prevalence of norovirus infection among Iranian patients with acute gastroenteritis is lower. Reasons for this results variation may be due to differences in the study population, detection methods, study design, and analysis methods. In previous studies, the prevalence of norovirus among inpatients was lower than among outpatients and the community (4, 30). Thus, one reason for the low prevalence of norovirus in our study may be due to the study populations of included articles, because most study populations of included articles were hospitalized patients.

A cross-sectional study was carried out for randomly selected children with acute gastroenteritis in Babylon Maternity and Children's Hospital and some primary health centers from June to November 2019, in Babylon, Iraq. The rapid Chromatographic Immunoassay was positive for rotavirus in 12.3%, norovirus in 0.8%, and astrovirus in 0% out of 130 stool samples. ELISA was positive for the rotavirus in 13.8%, followed by norovirus in 3.1% and none of the samples were positive for astrovirus. Gastroenteritis caused by rotavirus and norovirus was more common in males (72.7%) than in females (27.3%). Most rotavirus and norovirus infections were seen at the ages of 6 – 24 months (77.3%) (33). Another cross-sectional study was conducted for 93 children under the age of five years with acute gastroenteritis who attended the Emergency Department of Pediatrics at the Hospital for Maternity and Children in Baqubah City, Iraq. By using ELISA test the positive stool samples of rotavirus and norovirus were 79.6% and 1.1%, respectively. All norovirus cases were coinfected with Rotavirus (34). In a review conducted by Shoja Z et al, the mean prevalence of noro-

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virus associated with acute gastroenteritis was 6% in Iran (35). In comparison to the results of the mentioned studies conducted in Iran and neighboring countries, the pooled prevalence of norovirus infection among Iranian patients with acute gastroenteritis is higher.

In the present study, a significant difference in prevalence rates of norovirus infection was observed according to detection methods. In a study Immunochromatographic test (ICT) had low sensitivity but high specificity and accuracy for detecting norovirus. ICT could be a rapid and convenient test for the early identification of norovirus (11). In another study conducted in a University Hospital, in Turkey from September 2017 to May 2019, out of the 92 stool samples, 5 (5.4%) were positive for norovirus by ELISA and 12 (13%) by real-time RT-PCR (rRT-PCR), respectively. Thus rRT-PCR testing of stool samples for norovirus was more sensitive than ELISA (36). Detection of the viral nucleic acid by rRT-PCR will have a significant impact on the evaluation of virus burden and prevention of norovirus gastroenteritis in humans.

In eight included articles clinical findings were reported, such as fever, vomiting, diarrhea, abdominal cramps, respiratory symptoms, malaise, and myalgia. However, we could not analyze the pooled prevalence of norovirus infection according to gender, seasons of the year, and clinical findings among Iranian patients with gastroenteritis because of data incompleteness.

Overall, these research results provide a comprehensive overview of the prevalence of norovirus infection in different regions of Iran, taking into account various factors such as detection methods, geographical regions, age groups, years of study, and genogroups. This valuable information can help healthcare professionals and policymakers develop targeted strategies to prevent and control norovirus infections in Iran.

Conclusions

In conclusion, continuous monitoring of norovirus infection in the stool samples of patients with acute gastroenteritis is essential for managing to reduce the burden of norovirus-related gastroenteritis.

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Disclosure

None

Conflict of Interest

No conflict of interest is declared.

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Ethics Approval and Consent to Participate

This study was approved by Ethics Committee of the Kurdistan University of Medical Sciences (Approval No.:IR.MUK.REC.1401.285).

Data Availability Statement

All data generated or analyzed during this study are included in this article.

Authors' Contributions

Mazaher Khodabandehloo and Manouchehr Ahmadi Hedayati made an electronic literature search. A critical appraisal (CA) was performed by Mazaher Khodabandehloo, Manouchehr Ahmadi Hedayati and Yousef Moradi. Yousef Moradi analyzed the data. All authors contributed in interpretation of results and manuscript writing.

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