



# Systematic Review Seroprevalence of Hepatitis E Virus Infection in Middle Eastern Countries: A Systematic Review and Meta-Analysis

Fadi S. Qashqari 🕩

Department of Microbiology, College of Medicine, Umm Al-Qura University, Makkah 24381, Saudi Arabia; fsqashqari@uqu.edu.sa; Tel.: +966-553552660

Abstract: Hepatitis E virus (HEV) is a hepatotropic virus that is a major public health concern worldwide. Autochthonous HEV is spread through oral feces in unsanitary environments, as well as vertical and, occasionally, blood transfusion. HEV is more common in developing countries, but it has recently become more widespread in developed countries as well. The Middle East (ME) has long been an endemic location for HEV infection. Therefore, the aim of this systematic review and meta-analysis was to assess the seroprevalence of anti-HEV antibodies in ME countries. The author systematically searched five databases, namely ScienceDirect, EMBASE, Scopus, PubMed, and Google Scholar, to identify English-language articles published on or before 25 April 2022. Comprehensive meta-analysis software was used for all statistical analyses (CMA, version 3, BioStat, Englewood, CO, USA). After quality control and exclusion of irrelevant studies, 80 studies were included in the qualitative synthesis and meta-analysis. A forest plot showed that the overall pooled seroprevalence of HEV infection in ME countries in the fixed-effect and random-effect models were 21.3% (95% CI: 0.209-0.216) and 11.8% (95% CI: 0.099-0.144), respectively. Furthermore, the findings showed a high level of heterogeneity (I2 = 98.733%) among the included studies. In both fixed-effect and random-effect models, the seroprevalence of HEV infection by country was high in Egypt as compared to other regions, at 35.0% (95% CI: 0.342–0.359), and 34.7% (95% CI: 0.153–0.611), respectively. The seroprevalence of HEV infection by country was high among pregnant women, at 47.9% (95% CI: 0.459–0.499) in the fixed-effect model, and in renal transplant recipients, at 30.8% (95% CI: 0.222–0.410) in the random-effect model. The seroprevalence of HEV infection varies by country and study population in the Middle East. More research is needed to determine the disease's incidence, morbidity, and mortality in the region, where it is prevalent.

Keywords: hepatitis E virus; prevalence; Middle Eastern countries; systematic review; meta-analysis

# 1. Introduction

The World Health Organization (WHO) launched a global strategy to stop viral hepatitis transmission in 2016, recommending that persons with viral hepatitis have access to safe, accessible, and effective prevention, care, and treatment services [1]. By 2030, the goals are to reduce the number of new instances of hepatitis by 90 percent, treat 80 percent of eligible patients infected with viral hepatitis, and reduce the number of hepatitis-related fatalities by 65 percent [1]. Globally, nearly 1.34 million deaths were attributed to viral hepatitis in 2015, with 95 percent of those deaths attributed to chronic hepatitis B and C infections and the remainder to hepatitis A and E infections [1,2].

Global estimates suggest that more than 20 million new instances of hepatitis E virus (HEV) infections occur each year, with 3.3 million of those becoming symptomatic [3]. In 2015, the WHO reported 44,000 fatal HEV infections, accounting for about 3.3 percent of all viral hepatitis-related deaths [3].

HEV is a water- and food-borne illness that can cause severe epidemics in areas where sanitation is lacking [1,3]. However, there has been evidence of zoonotic and transfusion-related transmission [4,5]. Because there is no specific treatment for HEV infection, it is



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**Copyright:** © 2022 by the author. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https:// creativecommons.org/licenses/by/ 4.0/). managed mostly through supportive care [1,3]. Prevention, on the other hand, focuses on limiting exposure through improved sanitation, clean food and drinking water, and vaccination [1]. In comparison to hepatitis B and C, HEV infection is less likely to cause chronic liver damage, and the development of fulminant hepatitis, albeit rare, is mostly influenced by host-specific rather than virus-specific variables [6].

Clinical signs and symptoms such as myalgia, arthralgia, anorexia, hepatomegaly, fever, weakness, vomiting, and jaundice emerge two to nine weeks after HEV exposure. In rare and severe cases, HEV can cause abrupt liver failure. Chronic instances are uncommon; however, they can occur in immunocompromised persons [7,8]. There is a variety of laboratory tests for HEV infection diagnosis, which can be divided into direct (detection of HEV or viral protein via polymerase chain reaction or enzyme immunoassay) and indirect (detection of anti-HEV antibodies) approaches [9,10]. Recent HEV infection is linked to the existence of IgM anti-HEV antibodies. Furthermore, the presence of anti-HEV IgG antibodies is indicative of recent or distant HEV exposure. Both antibodies are critical for HEV infection diagnosis and can be linked to long-term infection [9,10].

The majority of people in Middle Eastern (ME) countries live in middle-income countries, where viral hepatitis is a major health concern [11]. Furthermore, HEV infection is highly endemic in most of the countries in this region [12,13]. Given these countries' changing socioeconomic conditions, identifying the epidemiological pattern of HEV infection will assist healthcare policymakers in making better decisions regarding future strategies for controlling this virus, as well as selecting and implementing cost-effective preventative methods [14,15].

Furthermore, to the very best of our knowledge, there remains a dearth of knowledge with respect to the prevalence of HEV-infected people with anti-HEV antibodies (IgG) in ME countries. Therefore, this systematic review and meta-analysis is the first attempt to provide a summarized and up-to-date estimation of the seroprevalence of HEV infection in ME countries.

#### 2. Materials and Methods

# 2.1. Data Sources and Literature Search Strategy

The author systematically searched five databases, namely ScienceDirect, EMBASE, Scopus, PubMed, and Google Scholar, to identify English-language articles published on or before 25 April 2022 that originally reported data on the prevalence of HEV infection in ME countries. The following keywords were used: "Hepatitis E virus", "HEV", and "Prevalence", combined with the names of ME countries, namely Akrotiri and Dhekelia, Bahrain, Cyprus, Egypt, Iran, Iraq, Israel, Jordan, Kuwait, Lebanon, Oman, Palestine, Qatar, Saudi Arabia, Syria, Turkey, United Arab Emirates, and Yemen.

The current systematic review and meta-analysis was conducted according to the PRISMA recommendations (Supplementary Material S1) and was registered with the International Prospective Register of Systematic Reviews (PROSPERO, registration No. CRD42022330216).

#### 2.2. Eligibility Criteria

The author included all observational studies conducted in ME countries that had, at least, an English abstract and reported on the prevalence of HEV-infected people with anti-HEV antibodies (IgG) among the general population, blood donors, hemodialysis patients, children, acute viral hepatitis patients, pregnant women, male blood donors, drug addicts, HIV positive individuals, thalassemia patients, soldiers, hemophiliac patients, renal transplant recipients, non-A-C hepatitis patients, and solid organ recipients. The systematic review and meta-analysis were designed to include people of all ages. Case reports, case series, letters, commentaries, editorials, non-human studies, symposia, correspondences, and citations without full text were all excluded from the study.

#### 2.3. Study Screening and Data Extraction

The article screening process and removal of duplicates were managed using EndNote V.X8 software. Furthermore, two researchers (F.Q. and S.K.) meticulously and manually treated the data to reduce the chance of duplication.

The following details were extracted from the included articles using a standardized data collection form: first-author name, publication year, study sample, study country, sampling year, study population, type of study, participants' age (range), study city, percentage of male participants, percentage of female participants, and prevalence of HEV-infected people with anti-HEV antibodies (IgG).

#### 2.4. Quality Assessment

The quality of the included articles was assessed using the National Institute of Health quality assessment technique [16,17]. This assessment tool was used because it allows for a thorough evaluation of the quality of the research included. Furthermore, the general quality of the studies was graded as good, fair, or poor, and these ratings were incorporated into the meta-analytic results. The two researchers (F.Q. and R.A.) compared their evaluations for each study, and any disagreements were handled through a joint discussion.

#### 2.5. Data Synthesis and Statistical Analysis

Comprehensive meta-analysis software was used for all statistical analyses (CMA, version 3, BioStat, USA). To reset the effect size value obtained from the meta-analysis, the fail-safe N approach was used to determine the number of studies that should be added to the meta-analysis. The average effect size of the meta-analysis studies was computed. The seroprevalence of HEV infection in ME countries was pooled and investigated using a random-effect model, with the results displayed in forest plots. Using the extracted data, the rate of events, their 95 percent confidence intervals, and their *p*-values were determined. The I<sup>2</sup> statistic was used to assess the degree of heterogeneity among the included studies, with I<sup>2</sup> values of 0–40%, 25–50%, 50–75%, and >75% indicating trivial, low, moderate, and high heterogeneity, respectively [18]. A non-significant degree of statistical heterogeneity, a random-effects model was adopted. A funnel plot was used to discover potential signs of publication bias between included papers, as detected by Begg's and Mazumdar's rank correlation tests.

## 3. Results

#### 3.1. Search Outcomes

The search yielded a total of 14,497 articles from five databases: ScienceDirect (n = 1816), EMBASE (n = 2326), Scopus (n = 2354), PubMed (n = 3328), and Google Scholar (n = 4673). After duplicates were excluded, 6539 articles remained. A further 3257 articles were excluded due to the studies being conducted in non-ME countries, in addition to 1965 studies deemed irrelevant after screening the titles and abstracts. Then, we reviewed the full text of the remaining 1317 articles and excluded 1237 studies for not fulfilling our inclusion criteria. Ultimately, 80 studies were included in the qualitative synthesis and meta-analysis. The PRISMA flow chart for the process of article screening and selection is presented in Figure 1.



Figure 1. PRISMA flow chart of study identification and study selection process.

## 3.2. Characteristics of the Included Studies

Of the 80 included studies, 41 were conducted in Iran, 14 in Turkey, 8 in Egypt, 4 in Israel, 3 in Saudi Arabia, 3 in Iraq, 2 in Qatar, 1 in Kuwait, 1 in Syria, 1 in Yemen, 1 in the United Arab Emirates, 1 in Lebanon, 1 in Palestine, and 1 in Jordan. The prevalence of HEV IgG antibodies in the included studies ranged from 0.8% to 84.3% (range = 14.9). The targeted populations in the included studies were the general population (15 studies), blood donors (12 studies), hemodialysis patients (12 studies), children (11 studies), acute viral hepatitis patients (8 studies), pregnant women (7 studies), male blood donors (3 studies), drug addicts (3 studies), HIV-positive individuals (3 studies), thalassemia patients (2 studies), soldiers (1 study), hemophilia patients (1 study), renal transplant recipients (1 study), non-A-C hepatitis patients (1 study), and solid organ recipients (1 study). The sample size of the included articles ranged from 43 to 11,604 (average = 844) (Table 1).

Publication Study Study Sampling Study Type of Participant Male Female Prevalence **First-Author Name** Study City Ref. Year Population Study Age (Range) (%) (%) (%) Year Sample Country Istanbul, Ayvalik, Aydin, General Cross-Thomas David 1993 1350 Turkey 1990-1992 18-65 years 50.2 49.8 5.9 [20] population sectional Trabzon region, and Adana Acute viral Cross-Abraham Koshy 1994 57 Kuwait 1992 19-46 years Kuwait 88 [21] 12 4 hepatitis patients sectional Hemophiliac Cross-Asher Barzilai 1995 188 9 [22] NM 2-75 years Tel Aviv 98.9 1.1 Israel sectional patients West Bank and General Cross-1995 1416 1988-1993 [23] Yuory Karetny Israel 1–66 years central region NM NM 2.6 population sectional of Israel Saudi Male blood Cross-Abdelaal Zawawi 593 1995 Jeddah 0 1998 15-60 years 100 16.9 [24] Arabia donors sectional Cross-[25] SI Abdel Hady 1998 95 Egypt NM Blood donors NM NM NM NM 45.2 sectional Cross-Hemodialysis 1998 [25] SI Abdel Hady 96 Egypt NM NM NM NM NM 39.6 sectional patients Acute hepatitis Hospital-Al-Azmeh J 1999 193 Syria 1995-1998 12-70 years Damascus 52.4 47.6 31.9 [26] patients based Six Cross-[27] Sıdal M 1997-1998 Children Istanbul NM 2001 909 Turkey months-15 NM 2.1sectional vears Pediatric age Cross-[28] Colak D 2002 338 Turkey 1996-1997 1–11 years Antalya NM NM 0.89 sectional groups Cross-Cesur Salih 2002 1046 Turkey 2000-2001 Adults 15–75 years Ankara NM 3.8 [29] NM sectional Arif Serhan Cross-2004 2000-2002 Pregnant women 19-42 years 0 76 100 12.6 [30] Turkey Afyon Cevrioglu sectional

Table 1. Characteristics of the included studies in the systematic review and meta-analysis.

First-Author Name	Publication Year	Study Sample	Study Country	Sampling Year	Study Population	Type of Study	Participant Age (Range)	Study City	Male (%)	Female (%)	Prevalence (%)	Ref.
Irfan Sencan	2004	383	Turkey	1999	Children	Cross- sectional	2–15 years	Düzce	51.7	48.3	4.7	[31]
Atabek Emre	2004	210	Turkey	2001–2002	Children	Cross- sectional	1–18 years	Konya	49	51	5.5	[32]
Aminiafshar S	2004	90	Iran	2003–2004	Blood donors	Cross- sectional	40–49 years	Tehran	80.2	19.8	7.8	[33]
Irfan Sencan	2004	93	Turkey	1999	Children	Cross- sectional	2–15 years	Golyaka	37.6	62.4	17.2	[31]
Serkan Oncu	2005	386	Turkey	NM	Pregnant women	Cross- sectional	18–32 years	Aydin	0	100	7	[34]
Alaa A Aboulata	2005	100	Egypt	2004–2005	Children presenting with minor hepatic disorders	Cross- sectional	1–10 years	Cairo	NM	NM	26	[35]
Mahnaz Taremi	2005	324	Iran	2004	Hemodialysis patients	Cross- sectional	18–80 years	Tabriz	59	41	7.4	[36]
Sonia Stoszek	2006	2428	Egypt	1997–2003	Pregnant women	Cross- sectional	18–40 years	Nile Delta	NM	NM	84.3	[37]
M. Taremi	2007	399	Iran	2004	Male blood donors	Cross- sectional	20–60 years	Tabriz	100	0	7.8	[38]
Gholam Ali Ghorbani	2007	800	Iran	2006	Soldiers	Cross- sectional	17–23 years	Tehran	100	0	1.1	[39]
Seyed Mohammad Alavi	2008	224	Iran	2005–2006	Drug addicts	Cross- sectional	18–54 years	Ahvaz	100	0	13.5	[40]
Mohammad Ali Assarehzadegan	2008	400	Iran	2005	Blood donors	Cross- sectional	18–60 years	Khuzestan	65	35	11.5	[41]
M. Taremi	2008	1824	Iran	2003	General population	Cross- sectional	6–80 years	Nahavand	NM	NM	9.3	[42]

First-Author Name	Publication Year	Study Sample	Study Country	Sampling Year	Study Population	Type of Study	Participant Age (Range)	Study City	Male (%)	Female (%)	Prevalence (%)	Ref.
Uçar Edip	2009	92	Turkey	NM	Hemodialysis patients	Cross- sectional	22–71 years	Hatay	58.7	41.3	20.6	[43]
Shamsizadeh Ahmad	2009	566	Iran	2006–2007	Children	Cross- sectional	6–15 years	Southwestern Iran	45.4	54.6	8.5	[44]
Behrooz Ataei	2009	816	Iran	2005	General population	Cross- sectional	6–60 years	Isfahan	47.5	52.5	3.8	[45]
Pourahmad Morteza	2009	43	Iran	2007	Hemodialysis patients	Cross- sectional	NM	Jahrom	67.4	32.6	7	[46]
Maral I	2010	515	Turkey	2003–2005	Primary school children	Cross- sectional	6–13 years	Ankara	52.7	47.3	1.9	[47]
Amen Ahmed Bawazir	2010	538	Yemen	2005	General population	Cross- sectional	one month– 79 years	Aden	52	48	16	[48]
Rachana Kumar	2010	469	United Arab Emirates	NM	Pregnant women	Cohort	NM	Al Ain	0	100	20	[49]
SG Sepanlou	2010	1423	Iran	2009	General population	Cross- sectional	NM	Tehran and Golestan	NM	NM	7.4	[50]
Turky Ataallah	2011	9610	Iraq	2005–2006	Acute viral hepatitis	Cross- sectional	1–60 years	Baghdad	49.5	50.5	19.4	[51]
Turky Ataallah	2011	6972	Iraq	2005–2006	General population	Cross- sectional	1–60 years	Baghdad	48.8	51.2	20.3	[51]
Zakieh Rostamzadeh Khameneh	2011	91	Iran	NM	Renal transplant recipients	Cross- sectional	6–65 years	Urmia	67	33	30.8	[52]
Seyed Reza Mohebbi	2012	551	Iran	2006–2007	General population	Cross- sectional	1–83 years	Tehran	36.3	63.7	9.4	[53]
Seyed Reza Mohebbi	2012	551	Iran	2006–2007	General population	Cross- sectional	1–83 years	Tehran	50	50	9.3	[53]

First-Author Name	Publication Year	Study Sample	Study Country	Sampling Year	Study Population	Type of Study	Participant Age (Range)	Study City	Male (%)	Female (%)	Prevalence (%)	Ref.
Abdolreza Sotoodeh Jahromi	2013	477	Iran	2009	Blood donors	Cross- sectional	17–59 years	Jahrom	447	30	5.4	[54]
Sanaz Ahmadi Ghezeldasht	2013	1582	Iran	2012	General population	Cross- sectional	1–90 years	Mashhad	45.4	54.6	14.2	[55]
Nural Cevahir	2013	185	Turkey	NM	Primary school children	Cross- sectional	7–14 years	Denizli	50.3	49.7	12.4	[56]
Hassan Ehteram	2013	530	Iran	2012	Blood donors	Cross- sectional	31–50 years	Central province	91.9	8.1	14.3	[57]
Omid Zekavat	2013	80	Iran	2010	Patients with chronic maintenance hemodialysis	Cross- sectional	26–80 years	Southwestern Iran	63.7	63.3	6.3	[58]
A.R. Mobaien	2013	93	Iran	2011	Hemodialysis patients	Cross- sectional	16–88 years	Tehran	52.7	47.3	26.9	[59]
Ayman Khalid Johargy	2013	900	Saudi Arabia	2009	Male blood donors	Cross- sectional	18–66 years	Makkah	100	0	18.7	[60]
Nawal Utba	2013	270	Iraq	NM	Blood donors and cleaning workers	Cross- sectional	18–60 years	Baghdad	67	33	21.5	[61]
Amitis Ramezani	2013	100	Iran	2012	HIV-positive individuals	Cross- sectional	34–43 years	Tehran	71	29	10	[62]
Fariba Keramat	2014	131	Iran	2011–2012	Injection drug users	Cross- sectional	22–70 years	Hamadan	99.2	0.8	6.1	[63]
Fariba Keramat	2014	131	Iran	2011–2012	Non-injection drug users	Cross- sectional	20–45 years	Hamadan	99.2	0.8	1.5	[63]
Seyed Seifollah Beladi Mousavi	2014	47	Iran	NM	Hemodialysis patients	Cross- sectional	20–80 years	Ahvaz	57.4	42.6	10.6	[64]
Peyman Eini	2015	153	Iran	2010	Hemodialysis patients	Cross- sectional	10–70 years	Hamadan	54.2	45.8	19.2	[65]

First-Author Name	Publication Year	Study Sample	Study Country	Sampling Year	Study Population	Type of Study	Participant Age (Range)	Study City	Male (%)	Female (%)	Prevalence (%)	Ref.
Orna Mor	2015	729	Israel	2009–2010	General population	Cross- sectional	10–75 years	Tel-Aviv	54	46	10.6	[66]
Mojgan Mamani	2015	1050	Iran	2010–2012	Pregnant women	Prospective cross- sectional	14–49 years	Hamadan	0	100	7.4	[67]
Seyed Moayed Alavian	2015	274	Iran	2012	Hemodialysis patients	Cross- sectional	21–80 years	Isfahan	52.9	47.1	9.9	[68]
Hassan Joulaei	2015	158	Iran	2012–2013	HIV-positive individuals	Cross- sectional	1–60 years	Shiraz	76.9	23.1	16.4	[69]
Behrouz Naeimi	2015	628	Iran	2013	Blood donors Cross- sectional 19-0		19–65 years	Bushehr	95.2	4.8	16.7	[70]
Daniela Ram	2016	49	Israel	2013–2015	Acute hepatitis patients	Cross- sectional	NM	Haifa, Tel Aviv, Beer Sheva	NM	NM	6.1	[71]
Hossein Keyvani	2016	200	Iran	NM	Blood donors	donors Sectional		Tehran	58.2	41.8	4.5	[72]
Hossein Keyvani	2016	100	Iran	NM	Patients with hepatitis C	Cross- sectional	20–61 years	Tehran	58.2	41.8	7	[72]
Hossein Keyvani	2016	150	Iran	NM	Patients with hepatitis B	Cross- sectional	20–61 years	Tehran	58.2	41.8	11.3	[72]
Hajiahmadi Nazila	2016	149	Iran	NM	Hemodialysis patients	Cross- sectional	15–90 years	Golestan	49	51	4	[73]
Hajiahmadi Nazila	2016	102	Iran	NM	HIV-infected patients	Cross- sectional	17–54 years	Golestan	68.6	31.4	33.3	[73]
Khashayar Hesamizadeh	2016	559	Iran	2014	Blood donors	Cross- sectional	18–37 years	Tehran	95.9	4.1	8.1	[74]
Zohreh Azarkar	2016	340	Iran	2013–2014	Blood donors	Cross- sectional	20–40 years	Birjand	93.8	2.2	14.7	[75]
Gamal Hasan	2016	123	Egypt	2007–2008	Children	Multicenter prospective	2–18 years	Assiut	59.3	40.7	26.8	[76]

	Tabl	<b>e 1.</b> Cont.										
First-Author Name	Publication Year	Study Sample	Study Country	Sampling Year	Study Population	Type of Study	Participant Age (Range)	Study City	Male (%)	Female (%)	Prevalence (%)	Ref.
Gülsüm İclal Bayhan	2016	408	Turkey	2014	Children	Cross- sectional	2 months- 18 years	Van	43.9	56.1	4.2	[77]
Gheyath Nasrallah	2017	5854	Qatar	2013–2016	Blood donors	Cross- sectional	15–80 years	Al Doha	97.4	2.6	20.7	[78]
Mohammad Obaidata	2018	450	Jordan	2015–2016	Patients who visit healthcare clinics for routine care	Cross- sectional	20–80 years	Eight governorates	45.1	54.9	30.9	[79]
Fatemeh Farshadpour	2018	1331	Iran	2016–2017	Pregnant women	Cross- sectional	14–45 years	Bushehr	0	100	6.3	[80]
Mehdi Parsa Nahad	2018	241	Iran	2013–2016	Acute viral hepatitis patients	Cross- sectional	10–80 years	Ahvaz	51.9	48.1	27.4	[81]
Najmeh Dalvand	2019	120	Iran	2019	Thalassemia- positive patients	Cross- sectional	17–45 years	Tehran	35	65	1.67	[82]
Mohammad Amin Behzadi	2019	562	Iran	2016–2017	Healthy individuals	Cross- sectional	1–86 years	Hormozgan	29.2	70.8	15.8	[83]
Doaa Abdelmawla	2019	140	Egypt	2016	Children with transfusion- dependent thalassemia	Cross- sectional	2–6 years	Mansoura	47.1	52.9	27.15	[84]
Mohamad Bachar Ismail	2020	171	Lebanon	2016	Hemodialysis patients	Cross- sectional	23–82 years	Tripoli	43.8	56.2	21.63	[85]
Azza Masoud Abdelbaky Ahmed	2020	11,604	Egypt	2013–2014	Blood donors	Cross- sectional	18–60 years	Qena	88.2	11.8	28.8	[86]
Mahbube Ouji	2021	226	Iran	NM	Hemodialysis patients	Cross- sectional	23–87 years	Bushehr, Borazjan, and Genaveh	56.2	43.8	68.6	[87]
Farzin Sadeghi	2021	247	Iran	2020	Pregnant women	Cross- sectional	17–42 years	Northern Iran	0	100	0.8	[88]

First-Author Name	Publication Year	Study Sample	Study Country	Sampling Year	Study Population	Type of Study	Participant Age (Range)	Study City	Male (%)	Female (%)	Prevalence (%)	Ref.
Reem A Al Dossary	2021	806	Saudi Arabia	2020	Blood donors	Cross- sectional	18–85 years	Eastern province	94.9	5.1	3.2	[89]
Sayed El-Mokhtar	2021	300	Egypt	2016–2018	Non-A-C hepatitis patients	Cross- sectional	40–60 years	Assiut	53	47	10	[90]
Enas Al Absi	2021	259	Qatar	2017–2019	Non-A-C hepatitis patients	Cross- sectional	6–98 years	Al Doha	61.4	83.6	32.1	[91]
Kamal Dumaidi	2022	432	Palestine	2015–2017	General population	Cross- sectional	1–86 years	West Bank and Jerusalem	49.3	50.7	3.7	[92]
Seval Öğüt	2022	485	Turkey	NM	Solid organ recipients	Cross- sectional	1–80 years	Izmir	64.7	35.3	17.3	[93]

NM denotes "not mentioned".

## 3.3. Overall Pooled Seroprevalence of Hepatitis E Virus Infection in Middle Eastern Countries

All eighty included studies were pooled for meta-analysis; the forest plot showed that the overall pooled seroprevalence of HEV infection in ME countries in the fixed-effect and random-effect models was 21.3% (95% CI: 0.209–0.216), and 11.8% (95% CI: 0.099–0.144), respectively. Furthermore, the findings showed a high level of heterogeneity ( $I^2 = 98.733\%$ ) among the included studies. Furthermore, the overall pooled seroprevalence of HEV infection in ME countries was statistically significant (pooled *p*-value < 0.001) in both fixed-effect and random-effect models (Figure 2). Table 2 shows the mean effect size and confidence intervals based on the random effect analysis of the studies in the meta-analysis.

Study name		Sta	listics for each	n study			E	vent rate and 95% CI		Weight (Fixed)	Weight (Random
	Event rate	Lower limit	Upper limit	Z-Value	p-Value	-1.00	-0.50	0.00	0.50 1.00	Relative weight	Relative weight
Thomas David et al. 1993	0.059	0.048	0.073	-23.985	0.000	1	- I	•	1 I	0.83	1.35
Abraham Koshy et al. 1994	0.035	0.009	0.130	-4.604	0.000			+		0.02	0.82
Asher Barzilai et al. 1995	0.090	0.057	0.141	-9.077	0.000			+		0.17	1.26
Yuory Karetny et al. 1995	0.026	0.019	0.036	-21.719	0.000			*		0.40	1.32
Si Abdel Hady et al. 1998a	0.453	0.356	0.553	-0.922	0.357				**	0.26	1.30
Abdelaal Zawawi et al. 1998	0.169	0.141	0.201	-14.546	0.000			+		0.91	1.35
ALAmmah Lat al 1999	0.336	0.303	0.437	4 953	0.043			- 1 - 7		0.25	1.30
Sidal M et al. 2001	0.021	0.013	0.000	16 592	0.000					0.20	1.28
Cesur Salih et al. 2002	0.038	0.028	0.052	-20.002	0.000			4		0.42	1.33
Infan Sencan et al. 2004a	0.047	0.030	0.073	-12.465	0.000			•		0.19	1.27
Aminiafshar S et al. 2004	0.078	0.038	0.154	-6.283	0.000			+		0.07	1.14
Atabek Emre et al. 2004	0.057	0.033	0.098	-9.430	0.000			+		0.12	1.23
Arif Serhan Cevrioglu et al. 2004	0.132	0.072	0.228	-5.561	0.000			+		0.10	1.19
lifan Sencan et al. 2004b	0.172	0.108	0.263	-5.719	0.000			+		0.15	1.25
Serkan Oncu et al. 2005	0.070	0.048	0.100	-12.966	0.000			+		0.28	1.30
Alaa A Aboulata et al. 2005	0.260	0.184	0.355	-4.588	0.000			-+		0.21	1.28
Mahnaz Laremi et al. 2005 Senia Sharanki ak al. 2005	0.0/4	0.050	0.108	-11,306	0.000			+		0.24	1.30
M Tatatri at al 2007	0.043	0.020	0.007	12 229	0.000			1	135	0.21	1.37
Sholam Ali Shorbani et al. 2007	0.011	0.000	0.021	-13 352	0.000					0.10	1 20 1
Seved Mohammad Alavi et al. 2008	0.134	0.095	0 185	-9.515	0.000			+		0.29	1.31
Mohammad Ali Assarehzadegan et al. 2008	0.115	0.087	0.150	-13.020	0.000			+		0.45	1.33
M. Tatemietal. 2008	0.093	0.081	0.107	-28.248	0.000			•		1.69	1.36
Shamsizadeh Ahmad et al. 2009	0.085	0.064	0.111	15.766	0.000			+		0.48	1.33
Pourahmad Morteza et al. 2009	0.070	0.023	0.195	-4.327	0.000			+-		0.03	0.93
UçarEdip et al. 2009	0.207	0.136	0.301	-5.226	0.000			+		0.17	1.26
Behvooz Ataei et al. 2009	0.038	0.027	0.054	-17.648	0.000			•		0.33	1.31
Maral I et al. 2010	0.019	0.010	0.036	-12.281	0.000			· .		0.11	1.21
SG Sepaniou et al. 2010	0.074	0.061	0.089	-24.949	0.000					1.07	1.35
Amen Anmeo Bawazir et al. 2010 Restaura Kumur et al. 2010	0.160	0.131	0.193	-14,100	0.000			+		0.79	1.30
Hachana Kumarerai. 2010 Turku Ataalish atal. 2011 a	0.200	0.167	0.239	-11.330 EE 214	0.000			Ţ		10.63	1.30
Turky Ataalah et al. 2011b	0.134	0.100	0.202	45 939	0.000					12 39	1.37
Zakieh Bostamzadeh Khameneh et al. 2011	0.308	0.134	0.410	-3 570	0.000					0.21	1.28
Seved Reza Mohebbi et al. 2012a	0.094	0.073	0.122	-15.518	0.000			+		0.52	1.33
Seyed Reza Mohebbi et al. 2012b	0.093	0.071	0.120	-15.530	0.000			+		0.51	1.33
Amitis Ramezani et al. 2013	0.100	0.055	0.176	-6.592	0.000			+-		0.10	1.20
NAWAL UTBA, 2013	0.215	0.170	0.268	-8.747	0.000			+		0.50	1.33
Ayman Khalid Johargy et al. 2013	0.187	0.163	0.213	-17.205	0.000			+		1.50	1.36
Sanaz Ahmadi Ghezeldasht et al. 2013	0.142	0.126	0.160	-24,964	0.000			•		2.12	1.36
Abdolreza Sotooden Jahromi and Morteza Pourahmad, 2013	0.055	0.037	0.079	-14.14/	0.000			*		0.27	1.30
Nural Caushir at al. 2013	0.145	0.110	0.170	.9.761	0.000			+		0.22	1.34
Omid B. Zekavat et al. 2013	0.063	0.026	0.142	-5.863	0.000			+		0.05	1.07
A.B. Mobaien et al. 2013	0.269	0.189	0.368	-4.278	0.000			+		0.20	1.28
Fariba Keramat et al. 2014a	0.061	0.031	0.117	-7.490	0.000			+		0.08	1.17
Seyed Seifollah Beladi Mousavi et al. 2014	0.106	0.045	0.231	-4.499	0.000					0.05	1.06
Fariba Keramat et al. 2014b	0.015	0.004	0.059	-5.847	0.000			+	1	0.02	0.82
Peyman Eini et al. 2015	0.190	0.135	0.259	-7.044	0.000			+		0.26	1.30
Hassan Joulaei et al. 2015	0.165	0.115	0.231	-7.572	0.000			+		0.24	1.29
Urna Mor et al. 2015	0,105	0.085	0.130	10.001	0.000					0.76	1.30
Reference Nacional at al 2015	0.033	0.000	0.140	15.014	0.000			-		0.27	1.30
Moinan Mamani et al. 2015	0.074	0.060	0.092	-21 436	0.000					0.391	135
Khathavar Hesamizadeh et al. 2016	0.081	0.061	0.106	-15.667	0.000			+		0.45	1.33
Zohreh Azarkar et al. 2016	0.147	0.113	0.189	-11,480	0.000			+		0.47	1.33
Daniela Ram et al. 2016	0.061	0.020	0.173	-4.582	0.000			+		0.03	0.94
Hajiahmadi, Nazila, et al. 2016a	0.040	0.018	0.097	-7.610	0.000	1		+	1	0.06	1.12
Gulsum Iclal Bayhan et al. 2016	0.042	0.026	0.066	-12.656	0.000			+		0.18	1.27
Hajiahmadi, Nazila, et al. 2016b	0.333	0.249	0.430	-3.300	0.001			+	1	0.25	1.30
Lamai Hasan et al. 2016	0.268	0.197	0.353	-4.930	0.000			+		0.27	1.30
Hossen Keyvani et al. 2016 Chaustic Neuralistic et al. 2017	0.073	0.003	0.101	-14.027	0.000			· ·		10.54	1.32
Fatemeh Fasthadhour et al. 2019	0.207	0.051	0.210	.23 932	0.000			1.1		0.96	1.37
Mohammad Dhaidata and Amira Boess 2018	0.309	0.268	0.353	-7 893	0.000			+		1.05	1.35
Mehdi Parsa Nahad et al. 2018	0.274	0.221	0.334	-6.751	0.000			+		0.53	1.34
Najmeh Dalvand et al. 2019	0.017	0.004	0.064	-5.718	0.000			+		0.02	0.82
Doaa Abdelmawla et al. 2019	0.271	0.204	0.351	-5.195	0.000			+		0.30	1.31
Mohammad Amin Behzadi et al. 2019	0.158	0.130	0.191	-14.458	0.000			+		0.82	1.35
Mohamad Bachar Ismail et al. 2020	0.216	0.161	0.284	-6.930	0.000			+		0.32	1.31
Azza Masoud Abdelbaky Ahmed et al. 2020	0.288	0.280	0.296	-44.151	0.000			1 1		26.13	1.37
Farzin Sadeghi et al. 2021	0.008	0.002	0.032	-6.772	0.000					0.02	0.83
Manbube Oujret al. 2021	0.686	0.622	0.743	5.448	0.000				+	0.53	1.34
Energia Aradosi et al. 2021 Sward El Moli Navat al. 2021	0.320	0.266	0.380	-5.645	0.000			· +		0.62	1.34
Reem à à Dossau et al 2021	0.100	0.0/1	0.139	17.001	0.000					0.30	1 20
Kamal Dumaidi wt al. 2022	0.032	0.022	0.047	-12 789	0.000			+		0.17	1.30
Seval Ogut et al. 2022	0.173	0.142	0.209	-13.027	0.000			+		0.76	1.35
Fixed	0.213	0.209	0.216	-124.850	0.000						
Random	0.118	0.099	0.141	-19.651	0.000			+			

**Figure 2.** Forest plot meta-analysis of seroprevalence of hepatitis E virus infection in Middle Eastern countries [20–93].

Model	1 Effect Size and 95% Confidence Interval				Test of Nu	ıll (2-Tail)		Hete	Heterogeneity			Tau-Squared		
Model	Number of Studies	Point of Estimate	Lower Limit	Upper Limit	Z-Value	<i>p</i> -Value	Q-Value	df (Q)	<i>p</i> -Value	I Squared	Tau Squared	Standard Error	Variance	Tau
Fixed	80	0.213	0.216	0.293	-124.850	0.000	6154 911	79	0.000	98 733	0.763	0.372	0.138	0.874
Random	80	0.118	0.141	0.253	-19.651	0.000	- 0101.711	.,	0.000	>0.700	0.700	0.072	0.100	0.07 1

 Table 2. Meta-analysis and effect analysis values of included studies, homogeneous distribution value, average effect size, and confidence intervals.

# 3.4. Subgroup Analysis

In both fixed-effect and random-effect models, the seroprevalence of HEV infection by country was highest in Egypt as compared to other countries, at 35.0% (95% CI: 0.342–0.359) and 34.7% (95% CI: 0.153–0.611), respectively (Figure 3).

	Group by													
Model	Study country	Study name		Stali	stics for each s	itudy			Event rate and 35% LT		Hendu	al [Fored]	Headual (Separ	ate tauj
			Event rate	Lower fimit	Upper fmit	Z-Vakie	p-Value	-1.00 -0.	50 0.00 0	50 1.00	Std R	esidual	Std Residu	al l
	Egypt	SIAbdel Hady et al.	0.453	0.356	0.553	-0.922	0.357	1	-	+ 1	2.09	1	0.30	1
	Egypt	SI Abdel Hady et al.	0.396	0.303	0.497	-2.026	0.043		-		0.94	1	0.14	
	Egypt	Alaa A Aboulata et al. Sonia Stoszek et al. 2006	0.260	0.164	0.350	-4.588	0.000				43.76	-	1.59	1
	Egypt	Gamal Hasan et al. 2016	0.268	0.197	0.353	4.930	0.000				-1.90	1	-0.25	1
	Egypt	Doaa Abdelmawia et al	0.271	0.204	0,351	-5.195	0.000		-		-1.95	1	-0.24	1
	Egypt	Azza Matoud Abdelbaky	0.288	0.280	0.296	-44.151	0.000		- '		-34.60		-0.19	1
Fixed	Egypt	Supera criminariai en al	0.350	0.342	0.359	-32.973	0.000				0.24	-	1.01	
Flandom	Egypt		0.347	0.153	0.611	-1,141	0.254			-				
	Iran	Arrinialshar S et al. 2004 Malazza Tazarri et al. 2005	0.078	0.038	0.154	-6.283	0.000		+		-1.19		-0.34	
	Iran	M. Taremi et al. 2007	0.078	0.055	0.108	13.229	0.000				2.53	i	-0.37	1
	Iran	Gholam Ali Ghorbani et al.	0,011	0.006	0.021	-13.352	0.000				-7.39		-2.80	1
	Iran	Seyed Mohammad Alavi et	0.134	0.095	0.185	-9.515	0.000		+		0.72		0.42	1
	lian	Monammac Au M. Talemi et al. 2009	0.093	0.087	0.150	-28 248	0.000		1.		-3.53		-0.11	
	Iran	Shamsizadeh Ahmad et al.	0.085	0.064	0.111	-15 766	0.000		•		-2.51	ī	-0.25	1
	Iran	Pourahmad Morteza et al.	0.070	0.023	0.195	-4.327	0.000		+		-0.98	1	-0.42	1
	lian	SG Senaniou et al. 2003	0.038	0.027	0.054	-17.648	0.000		1.		-6.76		-1.36	
	Iran	Zakieh Rostamzadeh	0.308	0 222	0.410	-3 570	0.000				5.29		1.77	1
	Iran	Seyed Reza Mohebbi et	0.094	0.073	0.122	-15.518	0.000		+		-1.78	1	-0.09	
	tran	Seyed Reza Mohebbi et Amilia Ramazani et al	0.093	0.071	0.120	-15.530	0.000		1		-1.91		-0.12	
	Iran	Sanaz Ahmadi	0 100	0.055	0.176	-24.964	0.000				3.11		0.52	1
	Iran	Abdolreza Soloodeh	0.055	0.037	0.079	-14.147	0.000		•		-4.24	1.	-0.86	- E
1	lian	Hassen Ehlerem et al.	0.143	0.116	0.176	-14.421	0.000		+		1.80		0.53	1
L	Iran	A.R. Mobaien et al. 2013	0.063	0.026	0.142	-6.863	0.000		÷		4.32	1	1.52	1
L	Iran	Fariba Keramat et al.	0.061	0.031	0.117	-7.490	0.000		+		-2.00	1	-0.65	1
	Iran	Seyed Seifollah Beladi	0.106	0.045	0.231	-4.499	0.000				-0.26	1	0.07	
1	Iran	Panba Keramat et al. Poiman Eini et al. 2015	0.015	0.004	0.059	-5.847	0.000		· -		-3.03		-1.92	1
L	Iran	Hassan Joulaei et al. 2015	0.165	0.135	0.231	-7.572	0.000		+		1.79	i	0.73	1
L	Iran	Seyed Moayed Alavian et	0.099	0.068	0.140	10.921	0.000		+		-1.03	1	-0.03	15
	Iran	Behrouz Naeimi et al	0.167	0.140	0.198	-15.014	0.000		.*		3.85	1.1	0.78	1
	Iran	Khashavar Hesamizadeh	0.074	0.061	0.092	-21.436	0.000				-4.50		-0.44	
	Iran	Zohreh Azerkar et al. 2015	0.147	0.113	0.189	11.480	0.000		+		1.64	1	0.57	1
	Iran	Hajahmadi, Nazila, el al	0.040	0.018	0.087	-7.610	0.000		+		-2.80	1.1	-1.15	1
	Iran	Hajahmadi, Nazla, et al Hostein Kenstani et al	0.333	0.249	0.430	-3 300	0.001				6.30		1.93	1
	Iran	Fatemeh Fatchadpour et	0.063	0.051	0.078	-23.932	0.000				6.30		-0.67	1
	Iran	Mehdi Parsa Nahad et al.	0.274	0.221	0.334	-6.751	0.000		-		7.25		1.60	0.0
	Iran	Nameh Dalvand et al.	0.017	0.004	0.064	-5.718	0.000		÷		-2.91		-1.83	1
	Itan	Farzin Sadechi et al. 2021	0.008	0.002	0.131	-6 772	0.000				-3.95		-2.54	1.1
	Iran	Mahbube Ouji et al. 2021	0.686	0.622	0.743	5.448	0.000		1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	+	19.76		3.92	- 1 I
Fixed	Itan		0.119	0.113	0.124	-78.424	0.000							
Handom	Iran	Turky Alastah at al.	0.101	0.080	0.126	-16.989	0.000				.1.52		.1.26	
	Iraq	Turky Ateallah et al.	0.203	0.194	0.213	-45 939	0.000				1.35	1	1.06	1
	Iraq	NAWAL UTBA, 2013	0.215	0.170	0.268	-8 747	0.000		+		0.70	i	0.68	1
Fixed	Iraq		0.198	0.192	0.204	-72.339	0.000							
mandom	Istael	Asher Batzilai et al. 1995	0.090	0.057	0.206	-9.077	0.000		+		1.25	1	0.52	1
	Istael	Yuory Karelny et al. 1995	0.026	0.019	0.036	-21.719	0.000				-7.23		-1.27	1
	trael	Orna Mor et al. 2015	0.106	0.085	0.130	-17.728	0.000				5.86		0.78	1
Freed	Israel	Dariela halli et al. 2016	0.069	0.058	0.061	-4.562	0.000			_	-0.21		-0.03	
Random	Israel		0.063	0.027	0.139	-6.048	0.000		+					
	Jordan	Mohammad Obaidata and	0.309	0.268	0.353	-7.893	0.000		+		4.96			
Feed	Jordan		0.309	0.268	0.353	-7.893	0.000		+					
es de Materia	Kuwait	Abraham Koshy et al.	0.035	0.009	0.130	-4.604	0.000		+		-2.79	1		
Fixed	Kuwait		0.035	0.009	0.130	-4.604	0.000		+-					
Random	Kuwai		0.035	0.009	0.130	-4.604	0.000		+		010			
Fixed	Lebanon	monalitied stachar islinat et	0.216	0.161	0.284	-6.930	0.000		1		0.12			
Random	Lebanon		0.216	0.161	0.284	6.930	0.000		+					
-	Palestine	Kamal Dumaidi wt al. 2022	0.037	0.023	0.060	-12.789	0.000		+		-7.66			
Pixed Random	Palestine		0.037	0.023	0.060	·12.769	0.000		1					
THE REPORT	Qalar	Gheyath Nassallah et al.	0.207	0.197	0.218	-41.631	0.000				4.32	1	-1.00	1
8. 18-	Qalar	Enas Al Absi et al. 2021	0.320	0.266	0.380	-5.645	0.000		+		4.32	1	1.00	1
Fixed	Qalar		0.212	0.202	0.223	41,789	0.000							
rendom	Saudi Arabia	Abdelaal Zawawi et al	0.169	0.162	0.382	-14 546	0.000				1.31	1	0.87	1
	Saudi Arabia	Ayman Khalid Johargy et	0.187	0.163	0.213	-17 205	0.000		-		4.22	i	1.07	i
-	Saudi Arabia	Reem A Al Dossary et al.	0.032	0.022	0.047	-17.061	0.000		•		8.95		-1.97	1
Random	Saudi Arabia		0.153	0.137	0.170	-26.793	0.000		+					
THE REAL PROPERTY.	Syria	Al-Azmeh J et al. 1999	0.321	0.259	0.390	-4.853	0.000		+		3.64	1		
Fixed	Syria		0.321	0.259	0.390	-4 853	0.000							
Handom	Syna	Thomas David et al. 1993	0.321	0.259	0.390	-4.853	0.000		+		.2.69		0.24	1
	Turkey	Sidal M et al. 2001	0.059	0.048	0.073	-26 365	0.000		L.		-5.97		-1.61	1
1	Tunkey	Cesur Salih et al. 2002	0.038	0.028	0.052	-20.002	0.000		•		4.77		-0.84	i
L	Tuikey	Irlan Sencan et al. 2004a	0.047	0.030	0.073	-12.465	0.000		+		-2.16		-0.54	1
L	Turkey	And Sethen Caution at all	0.057	0.033	0.098	9,430	0.000		*		-1.03	1	-0.27	1
L	Turkey	Irfan Sencan et al. 2004b	0172	0.108	0.263	5.719	0.000				3.45	1	1.27	1
1	Tunkey	Serkan Oncu et al. 2005	0 070	0.048	0.100	-12.966	0.000		+		-0.45	1	-0.00	
1	Tunkey	Upar Edip et al. 2009	0.207	0.136	0.301	5.226	0.000		·		4.59		1.56	1
L	Turkey	Nural Cevabriet al. 2013	0.019	0.010	0.036	-8.751	0.000		+		2.54		0.81	1
	Tunkey	Gulsum Icial Bayhan et al.	0.042	0.026	0.066	-12.656	0.000		•		-2.62	1	-0.70	1
P	Turkey	Seval Ogut et al. 2022	0 173	0.142	0.209	-13 027	0.000		-		8.77		1.35	1
Bandom	Turkey		0.076	0.069	0.084	46 025	0.000		+					
	United Arab	Rachana Kumar et al.	0.200	0.167	0.239	-11.995	0.000		+		-0.66	1		
Fixed	United Arab		0.200	0.167	0.239	-11.995	0.000		+					

Figure 3. Forest plot meta-analysis of seroprevalence of hepatitis E virus infection by country [20-93].

The seroprevalence of HEV infection by the study population was highest in pregnant women 47.9% (95% CI: 0.459–0.499) in the fixed-effect model and in renal transplant recipients, 30.8% (95% CI: 0.222–0.410) in the random-effect model, as compared to other populations (Figure 4).

Model	Group by Study population	Study name		Stati	tics for each r	study			E	veni rate and 95/ Cl		Weight (Fixed)	Weight (Separate tau)
			Event rate	Lower limit	Upper limit	Z-Value	p-Value	-1.00	-0.50	0.00 0.1	50 1.00	Relative weight	Relative weight
	Acute hepatilis	Abraham Koshy et al. 1994	0.035	0.009	0.130	4 504	0.000	1	1	- I		0.12	9.12
	Acute hepatitis	Al-Azmeh J et al. 1999	0.321	0.259	0.390	4 853	0.000			+		2.53	15 98
	Acute nepatitis	Letter Sami et al. 2002 Turkv Ataalah et al. 2011 a	0.194	0.186	0.052	-20.002	0.000			· .		90.17	15.52
	Acute hepatitis	Daniela Ram et al. 2016	0.061	0.020	0.173	4,582	0.000			+		0.17	10.62
	Acute hepalitis	Hossein Keyvani et al. 2016	0.073	0.053	0.101	-14.027	0.000			+		1.84	15.76
-	Acute hepalilis	Mehdi Passa Nahad et al. 2018	0.274	0.221	0.334	-6.751	0.000			+		2.88	16.05
Random	Acute hepahitis		0.188	0.181	0.195	-59 530	0.000			4			
Thereard	Blood donors	SI Abdel Hadviet al. 1998a	0.453	0.356	0.553	0 922	0.357					0 59	6341
	Blood donors	Abdelaal Zewawi et al. 1998	0.169	0.141	0.201	-14.546	0.000			+		2.08	7.02
	Blood donors	Ammalahar S et al. 2004	0.078	0.038	0.154	-6.283	0.000			+		0.16	4.68
	Blood donors	M. Larens et al. 2007 Mehanimud 65 Sciencebrade and at al.	0.115	0.065	0.108	13.229	0.000			<b>*</b>		1.021	6 50
	Blood donots	NAWAL UTBA 2013	0.215	0.170	0.269	-8.747	0.000			-		1.14	6 78
	Blood donots	Ayman Khalid Johargy et al. 2013	0.187	0.163	0.213	-17.205	0.000			+		3421	7.13
	Blood donois	Abdokeza Sotoodeh Jahromi and	0.055	0.037	0.079	-14.147	0 000			-		0.62	6.38
	Blood donors	Hassan Ehleram et al. 2013	0.143	0.116	0.175	-14.421	0.000			+		1.63	6.94
	Blood donots	Echarbaux Heramizadeb et al. 2015	0.081	0.061	0.156	-15.667	0.000					1.04	6 73
	Blood donots	Zohreh Azarkar et al. 2016	0.147	0.113	0.189	-11,460	0.000			+		1.07	6.75
	Blood donots	Gheyath Nasrallah et al. 2017	0.207	0.197	0.218	-41,631	0.000					24.08	7.30
	Blood donors	Azza Masoud Abdelbaky Ahmed el	0.288	0.280	0.296	-44.151	0.000					59.67	7.31
	Blood donors	Reem A.AJ Dossary et al. 2021	0.032	0.022	0.047	17.061	0.000					0.631	6,40
Fixed	Blood donors		0.240	0.234	0.245	+72.802	0.000			1.1			
anuom	Children	Sidal M et al. 2001	8.021	0.013	0.077	-16.592	0.000					9.60	10.06
	Children	Irian Sencan et al. 2004a	0.047	0.030	0.073	-12.465	0.000			•		8 85	10.02
	Children	Atabek Erre et al. 2004	0.057	0.033	0.098	9.430	0.000			+		5.84	9.73
	Children	Irlan Sencan et al. 2004b	0.172	0.108	0.263	-5.719	0,000			+		6.83	9.85
	Children	Alsa A Aboulata et al. 2005	0.260	0.184	0.355	-4.588	0.000			+-		9.92	10.09
	Children	Shamsizadeh Ahmad et al. 2009 Maud Let al. 2010	0.085	0.064	0.111	-15.766	0.000			*		22.66	10.39
	Children	Maran et al 2010 Noral Cestable et al 2013	0.019	0.010	0.036	-12.281	0.000			-		10.39	10.10
	Children	Gutum Icial Bashan et al. 2016	0.042	0.026	0.055	-12,656	0.000					8.40	9.99
	Children	Gamal Hasan et al. 2016	0.268	0.197	0.353	-4.930	0.000			+		12.45	10.18
Fixed	Children		0.068	0.077	0,100	-32,565	0.000			1			100
Random	Children		0.079	0.044	0.138	-7.670	0.000			+			
	Drug addicts	Seyed Mohammad Alavi et al. 2008 Sextex Kernerat et al. 2014a	0.134	0.055	0.185	-9.515	0.000			+		73.27	39.88
	Drug addicts	Faiba Keramat et al. 2014a	0.005	0.004	0.059	-7.430	0.000			F		5551	24.65
Fored	Drug addicts		0.102	0.075	0.136	-12.969	0.000			+		0.001	24.05
Random	Drug addicts		0.061	0.021	0.159	4.980	0.000			+			
	General population	Thomas David et al. 1993	0.059	0.048	0.073	-23.985	0.000			•		3.53	7.21
	General population	Yuony Kalelny et al. 1995	0.026	0.019	0.035	-21.719	0.000			1		1.69	7.00
	General population	M. Tarema et al. 2006 Reference Ataai et al. 2009	0.033	0.027	0.10/	-28.248	0.000					1.22	6.91
	General population	SG Sepaniou et al. 2010	0.036	0.061	0.034	-24 949	0.000					4 56 1	7.26
	General population	Amen Ahmed Bawazir et al. 2010	0.160	0.131	0.193	-14.105	0.000			+		3.39	7.20
	General population	Turky Ataslah et al. 2011b	0.203	0.194	0.213	-45.939	0.000			•		52.84	7.41
	General population	Seyed Reza Mohebbi et al. 2012a	0.094	0.073	0.122	-15.518	0.000			-		2.21	7.09
	General population	Seyed Heza Mohebbi et al. 2012b Casas Abmadi Ghazaidasid at al	0.142	0.071	0.120	-15.530	0.000			·.		217	7.09
	General population	Sanaz Anman Griezeloatrix et al. Orna Mor al al. 2015	0.142	0.085	0 130	17 728	0.000					3 23 1	7.19
	General population	Mohammad Obaidata and Amra	0.309	0.268	0.353	-7.893	0 000			+		4.50	7.26
	General population	Mohammad Amin Behzadi et al. 2019	0.159	0.130	0.191	-14,458	0.000			+		3.51	7.21
2004	General population	Kanal Dumaidi wt al. 2022	0.037	0.023	0.060	-12.789	0.000			•		0.72	6.50
Fixed	General population		0.000	0 148	0.159	-79.074	0.000			2			
narioom	Hemodelusis	SI Abdel Hadu et al. 1998b	0.036	0.303	0.132	-2 126	0.000			-		10.35	865
	Hemodiahan	Mahnaz Taremi et al. 2005	0.074	0.050	0.108	11,906	0.000			+		10.02	864
	Hemodialysis	Pourahmad Morteza et al. 2009	0.070	0.023	0.195	4.327	0.000			+		1.26	7.22
	Hemodialysis	UparEdip et al. 2009	0.207	0.136	0.301	-5 226	0 0 0 0					6 80	8 53
	Hemodialysis	Omid R. Zek avat et al. 2013	0.063	0.026	0.142	-5.863	0.000			+		211	7.61
	Hemodialysis	A.H. Mobaen et al. 2013 Second Second Name at al.	0.269	0.046	0.368	4.278	0.000					2.01	8 33
	Hemodalysis	Peyman Eini et al. 2015	0.190	0.135	0.259	-7.944	0.000			+		10.60	8 66
	Hemodialyzia	Seyed Moayed Alavian et al. 2015	0.099	0.068	0.140	-10.921	0.000			+		10.97	8.66
	Hemodielysis	Hajahmadi, Nazia, et al. 2016a	0.040	0.018	0.087	-7.510	0.000			+		2.60	7.99
	Hemodialysis	Mohamad Bachar Ismail et al. 2020	0.216	0.161	0.284	-6.930	0.000			*		13.07	B 70
Frond	Hernodalysis	manoube Ulup et al. 2021	0.966	0.522	0.743	10 000	0.000					21.96	8.78
Random	Hemodalyza		0.163	0.025	0.279	4 414	0.000						
	Hemophiliac patients	s Asher Barzilai et al 1995	0.090	0.057	0.141	-9.077	0.000			+		100.00	100.00
Fixed	Hemophiliac patients		0.090	0.057	0.141	-9.077	0.000			<b>T</b>			
Bandom	Hemophiliac patients	Andre Damanne et al comp	0.090	0.057	0.141	-9.077	0.000			+		10.00	20.72
	HIV positive	Hannan Joulaei et al. 2015	0.100	0.055	0.1/6	-5.592	0.000			+		40.69	30.73
	HIV positive	Hajahmadi Nazla, et al. 2015h	0.333	0.249	0.430	-3 300	0.001					42.46	34.70
Fixed	HIV positive		0.210	0.169	0.258	-9.687	0.000			+		and a second	
Bandom	HIV patitive		0 186	0.090	0.344	-3 483	0.000					- 500 400 - 10	
	Iranian coldiers	Gholam Ali Ghorbani et al. 2007	0.011	0.006	0.021	-13.352	0.000					100.00	100.00
Pred	Iranian soldiers		0.011	0.006	0.021	-13.352	0.000						
is anothin	Non-A-C becatile	Enas Al Absi et al. 2021	0.320	0.006	0.021	5.645	0.000					67.63	50.46
	Non-A-C hepatitis	Sayed El-Mokhtar et al 2021	0.100	0.071	0.139	-11,417	0.000			+		32 37	49 54
Fixed	Non-A-C hepatilis	water dance a contract of the	0.228	0.192	0.268	-11.138	0.000			+		200 March	SC3486
Random	Non-A-C hepalitis	WHEN IS ENTONIASIO	0.187	0.053	0.487	-2.031	0.042					1000000	10000
	Pregnani women	Ant Serhan Cevriogiu et al. 2004	0.132	0.072	0.229	-5,561	0.000	1	Į	+		1.49	14.24
	Pregnant women	Seikan Oncu et al. 2005	0.070	0.048	0.100	-12.966	0.000			•		4.31	14.41
	Pregnant women	Sonia Storzek et al. 2006 Barbara Kumar et al. 2010	0.843	0.828	0.857	30.134	0.000			1.00	×.	12 20	14.50
	Pregnant women	Mojpan Mamari et al. 2015	0.200	0.050	0.239	-71.535	0.000					12.38	14.4B
	Pregnant women	Falemeh Faruhadpour et al. 2018	0.063	0.051	0.078	-23.932	0.000					13 50	14.48
	Pregnant women	Farzin Sadeghi et al. 2021	0.006	0.002	0.032	-6.772	0.000			1		0.34	13.41
Fixed	Pregnant women	1194517.00047012001198035	0.479	0,459	0.499	-2.841	0.041						ALL ADAMATEST.
Random	Pregnant women		0.119	0.021	0.464	-2.112	0.035					100.0	100.00
Find	Henal transplant	Zakieh Rostamzadeh Khameneh el	0.308	0.222	0.410	-3.570	0.000					100.00	100.00
Bendom	Benal transplant		0.308	0,222	0.410	-3.570	0.000						
and the second h	Solid organ	Seval Ogut et al. 2022	0.173	0.142	0 209	-13.027	000 0			+		100.00	100.00
Fixed	Solid organ		0.173	0.142	0.209	-13.027	0.000			+			
Flandom	Solid organ		0.173	0.142	0.209	-13.027	0.000			+			
	Thalacsemia	Najmeh Dalvand et al. 2019	0.017	0.004	0.064	5.718	0.000			+		6.63	47.53
Fred	Thalassemia	Doae Abdelmawla et al. 2019	0.271	0.204	0.351	-5.195	0.000					93.37	52.47
Bandom	Thalassemia		0.233	0.175	0.303	-6.493	0.111			-			
Fried	Overall		0.213	0.209	0.216	-124 890	0.000						
_			0.610	0.000	0.0.0	1.000		_	_				

**Figure 4.** Forest plot meta-analysis of seroprevalence of hepatitis E virus infection by study population [20–93].

# 3.5. Publication Bias

The results of Begg's and Mazumdar's rank correlation tests revealed a dispersed distribution, implying publication bias. The *p*-values for Kendall's tau without continuity and Kendall's tau with continuity were both 0.001 (Table 3). Figure 5 depicts a funnel plot of the seroprevalence of HEV infection in ME countries with publication bias.

Kendall's S Statistic (P-Q)	6154.911	
Kendall's tau without co	ntinuity correction	
Tau	0.7633	
z-value for tau	-124.850	
<i>p</i> -value (1-tailed)	0.001	
<i>p</i> -value (2-tailed)	0.001	
Kendall's tau with cont	tinuity correction	
Tau	0.8737	
z-value for tau	-19.65	
<i>p</i> -value (1-tailed)	0.001	
<i>p</i> -value (2-tailed)	0.001	

Table 3. Begg's and Mazumdar's rank correlation.



**Figure 5.** Publication bias of the seroprevalence of hepatitis E virus infection in Middle Eastern countries.

## 4. Discussion

Worldwide, seroprevalence-based studies have received increased attention in recent years. However, due to incorrect diagnosis, underestimation, and a lack of awareness among clinicians about HEV, the published literature contains considerable gaps [94,95]. As a result, the goal of this study was to determine the seroprevalence of HEV infection in ME countries. Researchers and policymakers may benefit from the information in this systematic review and meta-analysis in order to better understand disease spread and develop effective control and prevention methods, particularly in ME countries.

Our findings showed that the seroprevalence of HEV infection in ME countries ranged from 0.8% among Iranian pregnant women [88] to 84.3% among Egyptian pregnant women [37]. Different test methodologies and geographic locations, research sample size, surveillance year, and other factors could explain these observed differences in HEV seroprevalence. However, in our study, in the fixed-effect and random-effect models, the overall pooled seroprevalence of HEV infection in ME countries was 21.3% and 11.8%, respectively. According to a recent systematic review and meta-analysis, the overall pooled prevalence of HEV infection in pregnant women around the world was 16.51% [95]. A

systematic review of HEV seroprevalence in thirteen African nations found that it ranged from zero to eighty-four percent, with pregnant women and rural areas having higher immunoglobulin levels than other areas [96]. The estimated pooled seroprevalence of HEV in Chinese blood donors was 30%. In European countries, the estimated seroprevalence of HEV ranged from 0.6% to 52.5% [97]. Another comprehensive evaluation of the Brazilian population found a 6.0% overall seroprevalence of HEV infection [98]. Furthermore, the pooled prevalence in our study is higher than in certain primary studies conducted among pregnant women in different countries, such as Serbian blood donors (15.0%) [99], as well as in Mexico (5.7%) [100], Pakistan (8.86%) [101], and Sudan (10.3%) [102].

Our analysis showed that Egypt has the highest seroprevalence of HEV infections compared to other countries. In Egypt, HEV infection is a neglected disease. In Egyptian hospitals, HEV testing is not frequently used for the diagnosis of suspected hepatitis patients [90]. Anti-HEV IgG seroprevalence in Egyptians is among the highest in the world, at up to 84 percent [37,103]. Furthermore, an HEV outbreak was previously observed in Assiut governorate rural villages [104].

Despite the fact that the incidence of HEV has declined significantly in recent years as a result of improved hygiene conditions [105], our analysis revealed that the seroprevalence of HEV infection was higher in pregnant women when compared to other populations. There is a considerable chance of vertical transmission of these viruses from the mother to the fetus, which can result in maternal and fetal problems, such as abortion, neonatal mortality, and early labor [106]. To avoid any negative consequences, it is critical to diagnose HEV infections in pregnant women.

An increasing number scientists and researchers are becoming aware of the repercussions of HEV infection, which include severe liver impairment and a high rate of morbidity and mortality, particularly in pregnant women. As a result, the pathophysiology and immunology of HEV interaction during pregnancy have received increased attention. However, especially in HEV endemic areas, it is critical to investigate genetic and environmental causes. To control and stop the disease in the near future, immunological research and prevention, as well as treatment measures, must be enhanced. In addition, in countries where the disease is endemic, cost-effective immunization efforts are required.

Despite the fact that the current meta-analysis has a large sample size and includes all ME countries and populations previously researched, it is subject to numerous limitations. The majority of the studies reviewed used distinct anti-HIV IgG ELISA kits with varying specificity and sensitivity, which could impair the reliability and accuracy of the tests. Only the anti-HEV IgG antibody level, which appears mainly after infection, was used to determine seroprevalence. Furthermore, the studies included in this systematic review and meta-analysis were observational, with a wide range of baseline characteristics, sample sizes, and sampling years.

## 5. Conclusions

The seroprevalence of HEV infection varies by country and study population in the ME and is highest in Egypt as compared to other countries and is highest in pregnant women and in renal transplant recipients as compared to other populations. More research is needed to determine the disease's incidence, morbidity, and mortality in the region, where it is prevalent. In addition, essential steps should be taken to control and prevent HEV infection in general and in pregnant women in particular. Visiting endemic areas requires extra attention, especially when it comes to drinking water and food safety.

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**Supplementary Materials:** The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/medicina58070905/s1, Supplementary Material S1: The PRISMA recommendations checklist [107].

**Institutional Review Board Statement:** The protocol of the study was registered with the International Prospective Register of Systematic Reviews (PROSPERO, registration No. CRD42022330216). Informed Consent Statement: Not applicable.

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