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Review

The burden of Hepatitis E virus in the Middle East and North Africa region: a systematic review

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Abstract

Introduction: Hepatitis E virus is a leading cause of hepatitis in the Middle East and North Africa region. Although several countries in this area were shown to be endemic for hepatitis E, little is known about the epidemiology and possible preventive measures. In this manuscript, we present the results of a systematic review addressing the seroprevalence of hepatitis E antibodies in the Middle East and North Africa region. Subsequently, we discuss the main prevention strategies for this virus.

Methodology: We performed a literature review using the PubMed Database of all the Studies reporting data on hepatitis E seroprevalence (Anti-hepatitis E IgM and IgG) among the 20 countries of the Middle East and North Africa region from January 2000 to July 2021.

Results: Eighty-nine articles were identified and included in our review. Ten of the MENA countries did not have any study that fits our criteria. Egypt and Iran were the countries with the highest IgG seroprevalence for hepatitis E reaching 85.1% and 68.6% respectively. Concerning acute hepatitis E presentations, Iraq and Egypt were shown to have the highest IgM seroprevalence reaching 38.1% and 35.3% respectively. Hemodialysis and poly-transfused patients as well as patients with concomitant hepatotropic viruses' infections were reported to have a higher seroprevalence than the general population.

Conclusions: Hepatitis E is a major healthcare problem in the endemic Middle East and North Africa region. Even though no definite prevention strategy was described until today, implementing multiple minor precautionary approaches could help reduce the virus spread.

Key words: Hepatitis E; MENA region; epidemiology; Middle East; North Africa; developing countries.

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Introduction

Hepatitis E virus (HEV) is a worldwide leading cause of viral hepatitis with an approximate lifetime prevalence of 12.5% [1]. Although HEV is a self-limiting disease in immunocompetent patients, it causes 3.3% of fatal viral hepatitis cases, and is therefore recognized as a major global public health problem [2]. In fact, this virus is known to be more likely prevalent in resource-limited environments with the most vulnerable population being pregnant women, neonates and organ transplant patients where the mortality can reach 25% [3]. The persistent neglect and under-estimation of this disease resulted in an upsurge of its prevalence, consequently causing an increase in HEV associated morbidity in the recent years. Since no specific treatment is currently available, the most effective way to decrease HEV's public health burden is to work on primary prevention strategies based on the specific epidemiology of each region. In fact, the modes of transmission depend on the concerned countries' resources. In The Middle East and North Africa (MENA) region, HEV is a major public health challenge because of the relatively high HEV prevalence along with the lack of advanced prevention strategies. We present in this manuscript an updated systematic literature review on the prevalence of HEV in the MENA region. On top of that, we briefly address the best prevention strategies that can help control its transmission.

Methodology

An electronic search of the literature was conducted using the PubMed database. We targeted all articles reporting epidemiologic hepatitis E data in all MENA countries. Search strategies included the following words: (Hepatitis E) AND (*MENA country name*). The MENA region - defined in 2021 by the United Nations Children's Emergency Fund (UNICEF) - encompass 20 countries that were all included in our search: Algeria, Bahrain, Djibouti, Egypt, Iran, Iraq,

Jordan, Kuwait, Lebanon, Libya, Morocco, Oman, Palestine, Qatar, Saudi Arabia, Sudan, Syria, Tunisia, the United Arab Emirates (UAE) and Yemen. Three investigators performed the search and data collection independently and included all data published before July 2021. All the resulting studies were screened. Original articles reporting HEV seroprevalence (anti-HEV immunoglobulin IgM and/or IgG) were included. Articles with untranslated abstracts written in non-English languages were excluded. Demographic data was collected and a descriptive analysis of the results was presented. Variables included were the following: mean age, number of participants, Anti-HEV IgM and Anti-HEV IgG.

Results

Supplementary Table 1 lists the studies that were included in our literature review (period of January 2000 to July 2021, among different MENA countries) with the size, nature, and mean age of the studied population as well its HEV seroprevalence (anti-HEV IgG and IgM). According to our inclusion criteria, no studies were found reporting the seroprevalence of HEV in the following countries: Bahrain, Djibouti, Kuwait, Libya, Morocco, Oman, Palestine, and Syria.

A study conducted in North Algeria among blood donors and outpatients showed an HEV IgG seroprevalence of 21.9% and 17.1% respectively [4]. In Egypt, a high seroprevalence was demonstrated in the early 2000s. A study conducted by Fix *et al*. in 2000 demonstrated an IgG seroprevalence of 67.7% [5]. More recent studies reported a markedly elevated seroprevalence as well. For instance, in a study by Elhendawy *et al*. in 2020, villagers with HCV were shown to have an HEV IgG seroprevalence of 71.4%. [6] Population-based reports of IgG seroprevalence in Egyptian rural areas were very variable depending on the region, ranging from 3.7% to 85.1% [5,7,8]. The prevalence of HEV among pregnant women seems to be worrisome as it reaches 84% in some rural areas such as the Nile Delta, as reported in the study by Stoszek in 2006 [9]. Intriguingly, the vertical transmission of the virus was described by El-Sayed Zaki *et al*. in 2013 through studying a group of 29 newborns with congenital hepatitis: 3% and 21% of were found to have anti-HEV IgM and IgG respectively while 3.4% and 31% of their mothers had positive IgM and IgG respectively. In Egypt, which is an endemic country for multiple hepatotropic viruses (hepatitis A, B or C virus), higher values of HEV seroprevalence were noted in cases of coinfection as demonstrated by multiple authors [6,10–12]. Moreover, wastewater treatment plants workers seem to be specifically at high risk of HEV with IgG values reaching 51% [13,14]. HEV also seems to be a significant cause of clinical and/or biological acute hepatitis in Egypt with anti-HEV IgM values reaching 83% [15–23].

In Iran, 32 epidemiological studies reported the seroprevalence of HEV among different population subgroups. In the general population, anti- HEV IgG values significantly varied between regions, ranging between 2.3% in a sample of the population of Sari district and 46.1% in a sample of the population of Southwest Iran [24–37]. This seroprevalence increased with time. The first studies an IgG seroprevalence of around 7% [36,38], whereas recent studies published in 2021 showed a seroprevalence of around 65% [39]. Six different authors reported anti-HEV IgG prevalence in hemodialysis patients in Iran and demonstrated values reaching 65.1% in a recent study conducted by Ouji *et al*. [30,38-43]. Seroprevalences in Iranian pregnant women were assessed by four studies [44–47]. The largest, done by Farshadpour *et al*. in 2018, included 1,331 asymptomatic pregnant women and showed 0.8% and 6.2% anti-HEV IgM and IgG prevalence respectively.

In Iraq, an outbreak that occurred in 2005 in Al Sadr Neighborhood, Baghdad, was described by Al-Nasrawi *et al*. where 38.1% of patients presenting with jaundice were found to be anti-HEV IgM positive [48]. A few years later, Utba *et al*. measured anti-HEV IgG levels in a sample from the same location and showed a seroprevalence of 21% [49].

The first report addressing the seroprevalence of HEV in Jordan was in 2018 and showed that 30.9% of randomly collected sera samples were HEV-IgG positive [50]. Two recent Lebanese studies reported a seroprevalence of 0.2% and 21.6% among pregnant women and hemodialysis patients respectively [3,51]. In Qatar, 20.5% of blood donors were found positive for HEV IgG antibodies in a study involving 5,854 blood donors [52].

In Saudi Arabia, a study conducted by Ayoola *et al*. in 2002 targeted a sample that included hemodialysis patients, inpatients, outpatients and healthy control individuals. While anti-HEV IgM prevalence was found to be significantly high in the hemodialysis population (4.8%), the IgG seroprevalence was surprisingly lower than that of other populations (10.6%, 12.5% and 10.8% for inpatients, outpatients and the control group respectively). Two studies aimed to measure blood donors anti-HEV IgG and IgM in Saudi Arabia and demonstrated seroprevalence of 4.3%

IgM ; 18.7% IgG in Makkah and 1.3% IgM ; 5.7% IgG in Qassim [53,54].

In South Sudan, the analysis of blood samples from a mass oral cholera vaccination campaign for displaced persons showed a high prevalence of HEV IgG positive individuals (75%) [55]. In fact, this country witnessed a recent HEV outbreak in 2012-2014 in Darfur. This outbreak was described by Elduma *et al*. in 2016, reporting an anti-HEV IgM prevalence of 32% [56]. HEV was also found in multiple symptomatic patients during a concomitant yellow fever and HEV outbreak (Darfur, 2012) with an anti-HEV IgM prevalence reaching 38% [57].

A Tunisian population-based study conducted in 2007 showed no anti-HEV IgM positive subjects and 4% IgG positive individuals among 1505 participants [58]. Anti-HEV IgG prevalence was also explored in different subgroups in this country and was found to be 29% in poly-transfused patients [59], 5.1-12% in pregnant women [60,61], 7.5% in hemophiliac patients, 10.2% in hemodialysis patients [62] and 3.8-19.5% in acute hepatitis patients [61,63].

In a study by Kumar *et al*. conducted in UAE, 20% of pregnant women were found to be IgM HEV positive [64]. Nevertheless, Abro *et al*. demonstrated that 40% of a sample of 122 acute hepatitis patients in UAE were HEV positive [65]. In Yemen, 10.7% of 356 polyclinics visitors were found to be IgG-HEV positive [66].

Discussion

The MENA region is known to be endemic for HEV but the global prevalence was hardly definable. This review is an update on the HEV epidemiology. According to our results, the HEV seroprevalence varies between the geographic areas of the region but the overall seroprevalence remains elevated in many countries where HEV epidemiology was investigated. For instance, Egypt and Iran were shown to be the most endemic countries for this virus. Worrisome numbers were recorded in Egypt, reaching an IgG seroprevalence of 85.1% in Egyptian villagers in 2006 [7] and an IgM seroprevalence of 83% in non HAV/HCV acute hepatitis patients in 2021 [23]. Iran was also shown to be an endemic region with IgM and IgG seroprevalence reaching 14.6% and 68.6% in hemodialysis patients in 2021 [39]. The importance of HEV as a public health concern has been much more considered from research and public health positions, and over the last decade, epidemiological studies on HEV in the MENA region have increased exponentially. One systematic review has already been published concerning the prevalence of HEV in the MENA region from 2000 until 2014 [67]. By this time, much more countries were left with no data. A significant number of studies has been published since 2014. Unfortunately, according to our results, recent studies showed an increase in HEV prevalence in many countries such as Egypt and Iran as previously mentioned. Other countries could be more prevalent for HEV but more studies are needed to confirm these findings. In addition, subcategories of pregnant women, hemodialysis patients, organ transplant patients, HIV patients and other immunosuppressed patients were shown to have significant numbers of HEV IgM and/or IgG when compared to the general population, despite being the most at risk-population with the highest mortality rate [68]. This highlights the lack of appropriate precautionary measures in these vulnerable populations. Very few studies investigated HEV in the pediatric population, the highest prevalence was reported in Egypt. More studies are needed to assess the impact of this virus on this particular population.

Multiple studies were performed on patients with acute hepatitis of no clear diagnosis, and HEV was shown to be highly prevalent in those patients. Hence, this virus is most often disregarded or not taken into account as much as it should be.

Overall, the burden of HEV in the MENA region could be explained by both its remarkable prevalence and continuous surge in some countries.

In order to alleviate this burden, we will now address the prevention strategies of the virus. Those strategies should be implemented according to the five means of transmission that have been identified for HEV until now.

Waterborne transmission is the predominant mode of transmission in developing countries. Practically, this includes recreational water use (bathing, swimming, water parks) and contaminated foods or beverages consumption. Thus, prevention here is based on ensuring access to safe water and sanitation. In addition, drinking water should be disinfected by boiling, filtration, chlorination and other treatment options [68].

Zoonotic transmission represents the virus transmission from animal species to humans. This is the primary mode of transmission of serotypes 3 and 4, rarely encountered in the MENA region. Hence, avoiding undercooked meat would be essential in preventing transmission from animals.

Parenteral transmission is another mode of transmission of HEV and consists of the contamination through a non-gastrointestinal route: transcutaneous, transmucosal (eyes, genitalia), respiratory,

bloodstream, urinary, aural or umbilical. Although less common than waterborne transmission, HEV transmission through blood transfusions has been described [69]. In fact, Nucleic Acid Testing screening of blood donors is applied in several industrialized countries and the cost-effectiveness of this technique is relatively acceptable [70]. Therefore, application of pre-transfusion blood screening programs should be a priority in developing countries, particularly when addressing immunocompromised patients and pregnant women in whom HEV can be fatal [71].

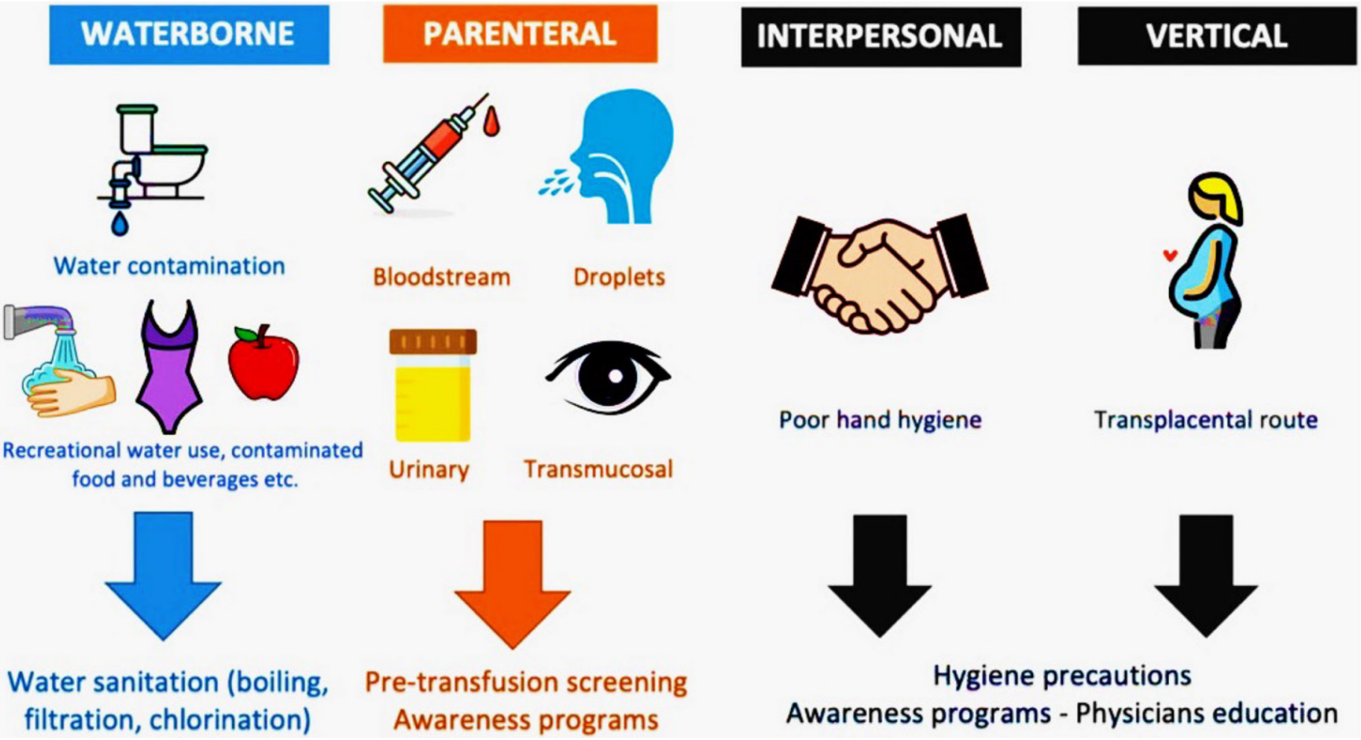
Moreover, an uncommon mode of transmission for HEV is person-to-person transmission. Poor hand hygiene, poor washing of kitchen tools and other similar behaviors increase the transfer of the virus from one person to another, particularly during outbreaks [72]. Thus, setting clear prevention practices and hygiene precautions can help avoid risky behaviors and habits, which can further reduce person to person transmission.

The last mode of transmission is the vertical transmission of the virus from mother to child that is mainly seen with serotype 1, leading to high prematurity and mortality rates in the mother or newborn. The exact mechanism of transmission remains until this day unclear [68].

Ultimately, raising awareness is imperative [2]. It can be achieved by scheduling HEV awareness programs and educating high-risk patients about the disease's symptoms and mechanisms of transmission. More importantly, the lack of knowledge concerning this disease amongst physicians is noticeable. An important number of cases go unrecognized, which potentially increases the environmental virus spread [73]. Educating clinicians about the importance of the inclusion of HEV in their routine differential diagnosis is another step forward. Figure 1 illustrates the main mechanisms of transmission of HEV serotypes 1 and 2 and the corresponding prevention strategies that can be applied in the MENA region.

Last but not least, there is no Foods and Drugs Administration (FDA)-approved vaccine for hepatitis E. However, a recombinant vaccine, HEV 239 (Hecolin), was approved in China in 2012 after a phase III randomized controlled trial against placebo [74]. The vaccine was found 86.8% effective for up to 4.5 years in all four genotypes. It was given in a three-dose schedule (0, 1, and 6 months) that was highly tolerated [75]. More data is needed to determine the safety and efficacy of this vaccine in high-risk populations. A promising phase IV randomized trial has been conducted in 2020 assessing the safety, immunogenicity and effectiveness of the vaccine in

Figure 1. Diagram illustrating the mechanisms of transmission of HEV serotypes 1 and 2 and appropriate prevention strategies in developing countries.



women of childbearing age [76]. The WHO did not make any recommendations yet for the routine use of this vaccine due to the lack of sufficient data [2]. Hopefully, with more upcoming studies, safe introduction of this vaccine in the MENA region could be a potential preventative approach.

Conclusions

The under diagnosis of hepatitis E is a major healthcare problem in the MENA region where several countries demonstrated a significantly high seroprevalence. The understanding of the disease's burden in this endemic area requires more solid epidemiological data. Even though no definite prevention strategy was described until today, implementing multiple minor preventive approaches could help reduce the virus spread.

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Annex – Supplementary Items

Supplementary Table 1. Summary of the literature review - studies reporting HEV seroprevalence among different countries of the MENA region.

First author / date	Ref.	Population	MA ± SD (years)	N	Anti-HEV IgM (%)	Anti-HEV IgG (%)
ALGERIA						
Behloul / 2016	[4]	Blood donors from North Algeria	39.3	379	0.5	21.9
		Outpatients from North Algeria		211	0	17.1
BAHRAIN						
-	-	-	-	-	-	-
DJIBOUTI						
-	-	-	-	-	-	-
EGYPT						
Fix / 2000	[5]	Nile Delta/Upper Egypt communities	26.5	10,026	-	67.7
			(20-40)*			50.9
El-Esnawy / 2000	[14]	Wastewater treatment plants workers	(41-50)*	205	-	43.2
			(51-60)*			46.2
El-Esnawy / 2001	[67]	Aborted women	-	-	3	22
Darwish / 2001	[9]	HCV-infected patients	35	321	-	56
		Control group	20	475	-	51
Stoszek / 2006	[8]	Pregnant women	(16-48) *	2,428	-	84.3
Stoszek / 2006	[7]	Egyptian Villagers	(5-75) *	919	-	3.7
El Sayed Zaki / 2006	[17]	Children with acute hepatitis	(6-12) *	64	17.2	12.5
		Control group	(6-12) *	16	0	12.5
Meky / 2006	[6]	Sample of rural Egyptian villages population	-	47	2.1	85.1
Zakaria / 2007	[21]	Clinical acute viral hepatitis patients	20.2 ± 14.2	200	12.5	-
		Children with positive anti-HAV IgM		44	4.5	34.1
		Positive HBV children		30	3.3	56.7
El Sayed Zaki / 2008	[12]	Positive HCV children	7.0 ± 2.0	50	0	52.0
		Children with combined HBV and HCV hepatitis		10	0	30.0
		Children with non-A/B/C virus hepatitis		28	0	7.1
El Sayed Zaki / 2009	[67]	Admissions to Children's Hospital	(6-12) *	68	35.3	2.9
Youssef / 2009	[20]	Patients with elevated liver enzymes	42.2 ± 8.6	214	2.3	-
Blackard / 2009	[15]	Acute viral hepatitis patients	-	287	20.2	-
Eldin / 2010	[16]	Symptomatic acute hepatitis patients	(1-65) *	235	16	-
Albatanony and El-Shafie / 2011	[13]	Wastewater treatment plants workers	47.1 ± 3.7	43	-	51
		Control group	48.2 ± 2.4	43	-	30
El Sayed Zaki and Othman / 2011	[19]	Patients with acute on chronic liver disorders	46.3 ± 8.8	100	5	30
Gad / 2011	[11]	Pregnant women with chronic HCV	32.5 ± 12.3	56	-	71.42
		Pregnant women without HCV	33.6 ± 7.8	60	-	47
El-Tras / 2013	[68]	Patients with history of jaundice	(20-40) *	134	-	38.1
		Newborns with signs of congenital hepatitis	0	29	3	21
El Sayed Zaki / 2013	[69]	Mothers of symptomatic newborns	26.2 ± 3.9	29	3.4	31
		Control group of newborns	0	29	0	0
		Mothers of control newborns	28.6 ± 7.0	29	0	0
Hasan / 2016	[18]	Children from Upper Egypt with acute viral hepatitis	6.4 ± 0.4	123	26.8	-
Abdelmawla / 2019	[70]	β-thalassemic children	(2-18) *	140	2.9	24.3
Elhendawy / 2020	[10]	Villagers with HCV	45.6 ± 9.5	505	0	71.4
El Sayed Zaki / 2020	[22]	Acute hepatitis pediatric patients	5.8 ± 3.5	180	5.6	25.6
Sayed / 2021	[23]	Non HAV/HCV acute hepatitis patients	51	30	83	43
El-Mokhtar / 2021	[71]	Infertile men	-	120	0	0
IRAN						
Taremi / 2005	[41]	Hemodialysis patients	53.5 ± 15.1	324	-	7.4
Taremi / 2007	[72]	Male blood donors in Tabriz	31.4 ± 9.8	399	-	7.8
Assarehzadegan / 2008	[73]	Blood donors	33.3	400	-	11.5
Taremi / 2008	[36]	Sample of the population of Nahavand	34.7 ± 19.5	1,824	-	9.3
Ataaei / 2009	[25]	Sample of the population of Isfahan Province	-	816	-	3.8
Saffar / 2009	[34]	Sample of the population of Sari district	(2-25) *	1,080	-	2.3
Sepanlou / 2010	[37]	Sample of Tehran and Golestan provinces populations	37.9 ± 13.4	1,423	-	7.4
Khameneh and Seperhvand / 2011	[74]	Kidney transplant patients	-	91	-	30.8
Mohebbi / 2012	[31]	Sample of the population of Tehran	41.3 ± 17.0	551	-	9.3
Raoofi / 2012	[33]	Patients from Khorramabad health centers	36	400	-	7.8
Ramezani / 2013	[75]	HIV-infected patients	38.6	100	0	10
		Control group	-	52	0	11.5
Ghezeldasht / 2013	[24]	Sample of the population of Mashhad	29.1 ± 18.5	1,582	-	14.2
Khameneh / 2013	[47]	Pregnant women	25.1 ± 14.9	136	-	3.6
Zekavat / 2013	[42]	Hemodialysis patients	55.7 ± 14.7	80	-	6.3

		Control group	51.7 ± 15.1	276	-	2.9
Mousavi / 2014	[39]	Hemodialysis patients	55.3 ± 8.1	47	-	10.6
Kelishadi / 2014	[30]	GB virus C patients on hemodialysis	54.3 ± 12.56	21	-	0
Eini / 2015	[40]	Hemodialysis patients	-	153	-	19.2
Farshadpour / 2015	[27]	Adults from South-West of Iran	45.9 ± 14.6	510	1.4	46.1
Asaei / 2015	[76]	Healthy individuals	6.5 ± 4.5	1,030	0.9	-
Alavian / 2015	[38]	Hemodialysis patients	59.9 ± 16.4	274	-	28.3
		Control group	46.6 ± 18.2	275	-	9.9
Joulaei / 2015	[77]	HIV-infected patients	39.1± 8	158	-	16.4
Naeimi / 2015	[32]	Blood donors	36.3	628	-	16.7
Hesamizadeh / 2016	[28]	Blood donors from Tehran	38	559	-	8.1
Jahromi / 2016	[78]	Thalassemia patients	15.2 ± 6	110	1.8	10
Jahanbakhsh / 2018	[29]	Homeless individuals	42	596	-	24.4
Farshadpour / 2018	[45]	Pregnant women	27.9 ±5.7	1,331	0.8	6.2
Behzadi / 2019	[26]	Patients presenting for check-up	35.7 ± 17.1	562	1.6	15.8
Kenarkoohi / 2020	[45]	Pregnant women	29.6	420	0.5	3.8
Shahriarirad / 2020	[79]	HIV-infected patients	40 ± 9.7	251	-	10.4
Sharifipour and Rad / 2020	[35]	Random individuals	41 ± 17.1	493	-	9.7
Ouji / 2021	[43]	Hemodialysis patients	60.3 ± 14.2	226	14.6	68.6
		Control group	58.6 ± 17.3	229	9.6	65.1
Sadeghi / 2021	[80]	Pregnant women	28.1 ± 5.3	247	-	0.8
IRAQ						
Chironna / 2003	[81]	Refugee Kurds from Iraq	24 ± 8.4	637	-	17.5
Myint / 2007	[82]	Thai troops deployed with United Nation peacekeeping forces in Iraq	(21 – 55) *	869	2.3	21.2
Al Nasrawi / 2010	[48]	Patients with jaundice during HEV outbreak in Al Sadr Baghdad	-	268	38.1	-
Al-Naaimi / 2012	[83]	Suspected acute hepatitis patients	-	2,692	1.6	-
Utba / 2013	[49]	Sample of the population of Al Sadr Baghdad	-	270	-	21
Merzah / 2019	[84]	Sample of the population of Karbala Governorate	(20-40) *	7,044	-	-
JORDAN						
Obaidat and Roess / 2018	[50]	Samples from populations of eight different governorates of Jordan	-	450	-	30.9
KUWAIT						
-	-	-	-	-	-	-
LEBANON						
Ismail / 2020	[3]	Sample of pregnant women in Northern Lebanon	28.3	450	-	0.2
Ismail / 2020	[51]	Hemodialysis patients	53.4 ±12.5	171	-	21.6
LIBYA						
-	-	-	-	-	-	-
MOROCCO						
-	-	-	-	-	-	-
OMAN						
-	-	-	-	-	-	-
PALESTINE						
-	-	-	-	-	-	-
QATAR						
Nasrallah / 2017	[52]	Blood donors	36.6 ± 9.3	5,854	0.6	20.5
SAUDI ARABIA						
Ayoola /2001	[85]	Patients with acute viral hepatitis	-	246	13.7	-
Ayoola /2002	[86]	Hemodialysis patients	39.0 ± 17.8	83	4.8	7.2
		Inpatients	49.8 ± 20.2	113	0	10.6
		Outpatients	42.5 ± 19.1	64	1.6	12.5
		Control group	40.3 ± 18.5	400	0.3	10.8
Khuroo /2004	[87]	Transfused group (Retrospective)	30.7 ± 17.3	145	6.2	9
		Non-transfused group (Retrospective)	27.1 ± 20.4	250	0.8	4
		Transfused group (Prospective)	31.5 ± 16.4	25	12	24
		Non-transfused group (Prospective)	29.5 ± 15.9	25	0	8
Johargy /2013	[54]	Male blood donors in Makkah	30 ± 7.8	900	4.3	18.7
Alhatlani /2021	[53]	Blood donors in Qassim	34.5 ± 10.3	1,078	1.3	5.7
SUDAN						
Mudawi and Yousif / 2007	[88]	Fulminant hepatic failure patients	38	37	5	-
Ahmed / 2008	[89]	Clinical acute hepatitis pregnant women	26.8 ± 7.1	16	50	-
Houcine / 2012	[90]	Blood donors	32.6 ± 8.6	687	-	5.4
		Acute hepatitis patients	39.0 ± 16.0	202	3.0	-
Elduma and Osman / 2014	[91]	Pregnant women from Eastern Sudan	26 ± 7.8	39	10.3	-
Elduma / 2016	[56]	Sporadic clinical hepatitis patients in North Kordofan	23.0 ± 14	432	23	-
		Acute hepatitis patients in Darfur	24.8 ± 12	152	32	-

Azman / 2017	[55]	Samples from a cholera vaccination campaign in South Sudan	(1-59) *	206	4	75
Ahmed / 2016	[57]	Suspected yellow fever patients in Darfur	25 ± 11	80	38	-
SYRIA						
-	-	-	-	-	-	-
TUNISIA						
Rezig / 2007	[58]	Population-based study	20.7 ± 2.0	1,505	0	4
Hannachi / 2011	[60]	Pregnant women	30.1 ± 6.0	404	0	12
Hannachi / 2011	[59]	Poly-transfused patients	-	107	-	28.9
		Control group	-	160	-	10
Hellara / 2014	[63]	Acute hepatitis patients	-	70	3.8	-
Ben-Ayed / 2015	[62]	Blood donors from Tunisia	42.2	426	-	4.5
		Hemophiliac patients	15.6	80	-	7.5
		Hemodialysis patients	54.86	286	-	10.2
Neffatti / 2017	[61]	Asymptomatic pregnant women	32 ± 8	216	1.4	5.1
		Patients with acute hepatitis	18 ± 22	92	0	19.5
UNITED ARAB EMIRATES						
Kumar / 2001	[64]	Pregnant women	25 ± 2.8	469	20	-
Abro / 2009	[65]	Acute hepatitis patients	29.2 ± 10.6	122	40	-
YEMEN						
Bawazir / 2010	[66]	Attendants of polyclinics	18.2 ± 19.4	356	-	10.7

N: population size; MA: mean age; SD: standard deviation; HCV: hepatitis C virus; HAV: hepatitis A virus; HBV: hepatitis B virus; HIV: Human Immunodeficiency Virus. * Mean age ± standard deviation unavailable, age range was provided instead.