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Epidemiology of hepatitis C virus among hemodialysis patients in the Middle East and North Africa: systematic syntheses, meta-analyses, and meta-regressions

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SUMMARY

We aimed to investigate hepatitis C virus (HCV) epidemiology among hemodialysis (HD) patients in the Middle East and North Africa (MENA). Our data source was an HCV biological measures database populated through systematic literature searches. Descriptive epidemiologic syntheses, effects meta-analyses and meta-regressions, and genotype analyses were conducted. We analyzed 289 studies, including 106 463 HD patients. HCV incidence ranged between 0 and 100% as seroconversion risk, and between 0 and 14·7 per 1000 person-years as incidence rate. The regional pooled mean estimate was 29·2% (95% CI: 25·6–32·8%) for HCV antibody positive prevalence and 63·0% (95% CI: 55·4–70·3%) for the viremic rate. Region within MENA, country income group, and year of data collection were associated with HCV prevalence; year of data collection adjusted odds ratio was 0·92 (95% CI: 0·90–0·95). Genotype diversity varied across countries with four genotypes documented regionally: genotype 1 (39·3%), genotype 2 (5·7%), genotype 3 (29·6%), and genotype 4 (25·4%). Our findings showed that one-third of HD patients are HCV antibody positive and one-fifth are chronic carriers and can transmit the infection. However, HCV prevalence is declining. In context of growing HD patient population and increasing HCV treatment availability, it is critical to improve standards of infection control in dialysis and expand treatment coverage.

Key words: Epidemiology, hemodialysis, hepatitis C, Middle East and North Africa, prevalence.

INTRODUCTION

Viral hepatitis is the 7th leading cause of mortality worldwide with hepatitis C virus (HCV) accounting for about half of this mortality [1]. Though HCV infection is a public health concern globally, the Middle East and North Africa (MENA) is the most affected region by this infection [1–3]. For 2015, MENA was estimated to have the highest incidence rate of all regions at 62·5 per 100 000 person-year, second largest incidence at 409 000 new infections per year, highest HCV antibody prevalence at 2·3%, and largest number of chronically infected people at 15 million [2].

Recent breakthroughs in HCV treatment, notably the introduction of highly effective direct-acting antivirals (DAA), have ushered a new era for controlling

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HCV and reducing its disease burden [4]. Global targets have been set to eliminate HCV and reduce its mortality by 2030 [5, 6].

HCV is a blood borne pathogen transmitted parenterally such as through sharing of injections and use of contaminated medical equipment [7]. Patients undergoing hemodialysis (HD) are at a higher risk of HCV exposure due to sharing of dialysis machines [8]. It has been estimated that HD increases the odds of acquiring HCV by five folds [9]. Characterizing HCV infection levels in HD patients and controlling its transmission through this mode of exposure are integral to improving the quality and healthcare utilization of HD. More specifically, this would lead to the prevention of unnecessary health complications such as liver disease and hepatic malignancies, and to a reduction in associated healthcare costs [10–12].

Against this background, we aimed to characterize HCV epidemiology among HD patients in the MENA region by: (1) systematically describing the evidence on HCV antibody incidence and prevalence in this population; (2) estimating the mean country-specific HCV prevalence in HD patients; (3) estimating HCV viremic rate in HD patients, that is the prevalence of HCV chronic infection (HCV RNA positivity) among antibody positive patients; (4) assessing associations with HCV prevalence in this population; and (5) assessing the frequency, distribution, and diversity of HCV genotypes in HD patients. This study was conducted under the umbrella of the MENA HCV Epidemiology Synthesis Project, an on-going effort to characterize HCV epidemiology and inform key public health research, policy, and programming priorities in MENA [13–19].

METHODOLOGY

Data source

Our source of data was the MENA HCV Epidemiology Synthesis Project database. This database consists of several sub-databases that include an HCV antibody incidence database comprising 47 incidence studies among 29 600 participants, an HCV antibody prevalence database comprising 2543 antibody prevalence studies among 52 598 736 participants, an HCV RNA prevalence (among antibody positive persons) database comprising 178 RNA prevalence studies among 19 593 HCV antibody-positive participants, and an HCV genotype frequency database comprising 338 HCV genotype studies among 82 257 participants.

The MENA HCV Epidemiology Synthesis Project database was compiled through systematic searches of the literature [13, 15–17, 20–22] informed by the Cochrane Collaboration handbook [23] and reporting the findings using the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines [24]. The searched literature included international databases (PubMed and Embase), regional databases, national databases, and the MENA HIV/AIDS Epidemiology Synthesis Project database [25, 26], in addition to gray literature comprised of public health reports and routine data reporting, which are available from the authors upon request. The systematic reviews used broad search criteria with no language or year restrictions, to capture all publications pertinent to HCV since the discovery of the virus in 1989 [27, 28]. The systematic searches screened for duplicate studies and excluded them to avoid double counting of any single study.

The definition of the MENA region in these searches and in the present article included the 24 countries of Afghanistan, Algeria, Bahrain, Djibouti, Egypt, Iran, Iraq, Jordan, Kuwait, Lebanon, Libya, Mauritania, Morocco, Oman, Pakistan, Palestine, Qatar, Saudi Arabia, Somalia, Sudan, Syria, Tunisia, the United Arab Emirates (UAE), and Yemen.

For the purpose of the present study, we also searched the literature (non-systematically) for studies of the population proportion of HD patients in MENA countries – that is the proportion of HD patients among the whole population in a given country. For estimating the number of people undergoing dialysis, the total population size in each country was obtained from the United Nations World Population Prospects database [29]. The MENA region estimate was calculated as a weighted (by population size) mean of available country measures.

Quantitative analyses

Meta-analyses

We conducted meta-analyses to estimate the country-specific mean HCV antibody prevalence. We further stratified HCV prevalence measures by year of publication and conducted meta-analyses for three different but consecutive temporal durations to descriptively examine changes in prevalence with time. Studies consisting of a minimum of 20 participants were included. We also conducted meta-analyses to estimate the

country-specific mean viremic rate. Studies consisting of a minimum of 10 antibody-positive participants were included. In the event that the study reported HCV prevalence by different strata, such as age and sex, among others, the total sample size was replaced with stratified measures whenever the sample size requirement was fulfilled for each stratum.

Meta-analyses were conducted whenever we had three or more measures to be pooled using a DerSimonian–Laird random-effects model with inverse variance weighting [30]. The variance was stabilized using the Freeman–Tukey type arcsine square-root transformation [31]. Cochran's Q test was implemented to assess evidence for heterogeneity in effect size; a P-value $< 0{\cdot}1$ was considered significant [32, 33]. The I^2 was calculated to assess the proportion of between-study variation in effect size (HCV prevalence or HCV viremic rate) that is due to actual differences in effect size between studies [32]. The prediction interval was calculated to assess the distribution of true effects around the estimated mean [32, 34].

Meta-regressions

We conducted meta-regressions on HCV prevalence studies to assess associations with HCV prevalence. Four types of potential predictors were specified *a priori* and included in the analyses: region within MENA, country income group, year of data collection, and sample size. Factors with a P-value $< 0{\cdot}1$ in univariable analyses were eligible for inclusion in the final multivariable model. Factors with a P-value $< 0{\cdot}05$ in the multivariable model were considered as significant predictors.

The region variable consisted of seven strata based on geographic proximity: Fertile Crescent (Iraq, Jordan, Lebanon, Palestine, and Syria); Gulf (Kuwait, Oman, Saudi Arabia, UAE, and Qatar); Horn of Africa (Yemen and Sudan); Maghreb (Algeria, Libya, Morocco, and Tunisia); Egypt; Iran; and Pakistan. This classification covers all MENA countries with available HCV data in HD patients.

The income group variable stratified countries according to their income group per World Bank classification [35]. Low middle-income countries included Egypt, Morocco, Pakistan, Sudan, Syria, Tunisia, and Yemen. Upper middle-income countries included Algeria, Iran, Iraq, Jordan, Lebanon, Libya, and Palestine. High-income countries included Kuwait, Oman, Saudi Arabia, Qatar, and UAE.

For the year-of-data-collection variable, we imputed the missing observations using the median of the observed values calculated by subtracting the year of data collection from the year of publication for each study. A sensitivity analysis was conducted with missing values for the non-imputed observations. The results were similar with no impact on statistical significance (Supplementary Table S1 on the Cambridge Journals Online website).

Genotype diversity

We analyzed the regional and country-specific frequency, distribution, and diversity of HCV genotypes among HD patients. The regional analysis was conducted based on actual frequency from available studies, and also as a weighted estimate by each country's population size. The frequency for each genotype was calculated with individuals testing positive for multiple genotypes contributing separately to the sum of cases for each genotype, as per earlier methodology [36]. Genotype diversity was assessed using Shannon Diversity Index [37].

Statistical analyses were conducted using R studio version 3.3.2 [38] and StataSE version 13 [39].

RESULTS

HD in MENA

The population proportion of patients undergoing HD varied across countries (Table 1). The lowest reported was 250·2 per million population in Bahrain, and the highest reported was 665·4 per million population in Lebanon. Based on available population proportions, we estimated the country-specific number of patients undergoing HD (Table 1). The lowest was 327 patients in Bahrain, and the highest was 25 225 in Iran. The MENA region population proportion was 383·6 per million population yielding an estimate of 239 759 HD patients.

Scope of evidence

Out of the MENA HCV Epidemiology Synthesis Project database, we identified 21 HCV incidence measures among a total of 8857 HD patients (Supplementary Table S2), 205 HCV antibody prevalence measures among a total of 92 341 HD patients (Table 2), 31 HCV RNA prevalence measures among a total of 3172 HCV antibody-positive HD patients (Supplementary Fig. S1), and 31 HCV

Table 1. *Population proportion of hemodialysis (HD) in the Middle East and North Africa (MENA)* [40]

Country	Prevalence of HD (per million population)	Total population	Estimated number of individuals on HD
Bahrain	250·2	1 306 000	327
Iran	322·8	78 144 000	25 225
Kuwait	403·2	3 753 000	1513
Lebanon	665·4	4 924 000	3276
Oman	285·9	4 236 000	1211
Qatar	330·6	2 172 000	718
Saudi Arabia	512·9	30 887 000	15 842
MENA[a]	383·6	625 023 000	239 759

[a] The population proportion of HD for the MENA region was estimated as a weighted mean of available country measures.

genotype frequency measures among a total of 2093 HCV RNA-positive HD patients (Table 6; Supplementary Fig. S2).

Out of the 24 included countries, data were available from 19 countries. The number of data points varied by country. Iran, Saudi Arabia, Tunisia, and Egypt contributed the largest number of data points. Several countries contributed as little as one data point.

HCV antibody incidence among HD patients

Egypt ($n = 6$), Lebanon ($n = 6$), and Morocco ($n = 4$) are the countries with the largest number of studies reporting HCV incidence among HD patients (Supplementary Table S2). Most studies had a follow-up duration ranging from 6 to 36 months, and reported incidence either as a risk of seroconversion or as an incidence rate. Seroconversion risk varied widely and was in the range of 0–100%. Incidence rate also varied substantially and was in the range of 0–14·7 per 1000 person-years. Incidence varied extensively even within the same country. For example, in Lebanon, HCV incidence rate varied from 0 to 14·7 per 1000 person-years across different geographical sites [120].

HCV antibody prevalence among HD patients

Iran ($n = 41$), Saudi Arabia ($n = 39$), and Egypt ($n = 26$) are the countries with the largest number of studies reporting HCV prevalence among HD patients (Table 2). HCV antibody prevalence varied widely within and across countries and was in the range of 0–100% with a median of 26·5%. For example, in Egypt, HCV prevalence varied from 10·0% to 100% across different geographical sites at different times.

Table 3 shows the pooled mean estimate of HCV prevalence by country, by temporal duration, and for the region. The country-specific mean estimate ranged from 7·3% (95% CI: 3·7–11·7%) in Lebanon to 65·5% (95% CI: 56·5–74·1%) in Egypt. HCV prevalence was 51·6% (95% CI: 46·1–57·1%) in years of publication 1989–1998, and decreased to 27·8% (95% CI: 23·1–32·8%) in 1999–2008, and 18·8% (14·5–23·5%) in 2009–2016.

The mean estimate for the region was 29·2% (95% CI: 25·6–32·8%). Egypt, Syria, Saudi Arabia, Yemen, Morocco, and Qatar had a mean estimate exceeding 40%. There was strong evidence for heterogeneity in effect size (that is HCV prevalence) in all countries ($P \leqslant 0{\cdot}01$). The vast majority of the variation was due to variation in effect size rather than chance ($I^2 > 50\%$). The prediction intervals confirmed substantial variation in effect size in each country. Forest plots for the country-specific meta-analyses can be found in Supplementary Fig. S3.

HCV viremic rate among HD patients

Tunisia ($n = 13$) is the country with the largest number of studies reporting HCV viremic rate among HD patients (Table 4). For the rest of the countries, there were either few or no measures. HCV viremic rate varied across studies and was in the range of 19·1–93·3% with a median of 65·4%. The pooled mean estimate for HCV viremic rate across MENA was 63·0% (95% CI: 55·4–70·3%). There was evidence for heterogeneity in effect size estimates (here HCV viremic rate) across the region with a $P < 0{\cdot}0001$. The I^2 for the pooled estimate was indicative of the variation being due to true differences in effect size rather than chance ($I^2 = 94{\cdot}0\%$). The prediction interval confirmed substantial variation in effect size. Forest plot for the regional meta-analysis can be found in Supplementary Fig. S1.

Associations with HCV antibody prevalence among HD patients

Table 5 shows the results of the univariable and multivariable meta-regressions. Region, income group, and year of data collection were associated with HCV antibody prevalence in the univariable analysis (*P*-value

Table 2. *Studies reporting hepatitis C virus (HCV) antibody prevalence among hemodialysis patients across the Middle East and North Africa*

First author, year of publication	Year(s) of data collection	Study site	Population	Sample size	HCV prev. (%)
Algeria ($n = 3$)					
Algerian Ministry of Health, 2008 [41]	2008	–	HD patients	2503	23·8
Afredj, 2009 [42]	1995	–	HD patients	1225	42·0
Zitouni, 2010 [43]	2008–2009	Clinical setting	HD patients	373	22·8
Egypt ($n = 26$)					
Abdel Hady, 1999 [44]	–	Unspecified	HD patients	96	27·1
Abdel-Wahab, 1994 [45]	1992	Clinical setting	HD patients	78	46·2
Attia, 2010 [46]	2008–2009	Clinical setting	HD patients	206	46·1
El Gohary, 1995 [47]	1990–1992	Clinical setting	HD patients	108	70·4
El Sayed Zaki, 2013 [48]	–	Unspecified	HD patients	30	10·0
El-Emshaty, 2011 [49]	–	Clinical setting	HD patients	39	56·4
Elgohry, 2012 [50]	–	Clinical setting	HD patients	25	72·0
Gohar, 1995 [51]	–	Unspecified	HD patients	64	87·5
Goher, 1998 [52]	–	HD center/units	Male HD patients on non reused dialyzers	131	75·6
Goher, 1998 [52]	–	HD center/units	Female HD patients on non-reused dialyzers	39	79·5
Goher, 1998 [52]	–	HD center/units	Male HD patients on reused dialyzers	108	67·6
Goher, 1998 [52]	–	HD center/units	Female HD patients on reused dialyzers	57	66·7
Hammad, 2009 [53]	2008	Clinical setting	HD patients	34	94·1
Hassan, 1993 [54]	1991–1993	Unspecified	HD patients	105	73·3
Helaly, 2015 [55]	2012	HD center/units	HD patients	100	34·0
Mouchiran, 1995 [56]	–	Unspecified	Patients regularly attending renal dialysis units (controlled units)	250	68·0
Mouchiran, 1995 [56]	–	Unspecified	Patients regularly attending renal dialysis units (not controlled units)	100	98·0
Ibrahim, 2010 [57]	2007	Clinical setting	HD patients	100	70·0
Ismail, 1994 [58]	–	Clinical setting	HD patients for <1 year	25	72·0
Ismail, 1994 [58]	–	Clinical setting	HD patients for >1 year	39	100
Kamal, 2013 [59]	2011	Clinical setting	HD patients	170	60·6
Kandil, 2007 [60]	2004–2006	Clinical setting	HD patients	31	51·6
Khodir, 2012 [61]	2011	Clinical setting	HD patients	2351	35·0
Saddik, 1997 [62]	–	Clinical setting	HD patients	50	72·0
Shatat, 2000 [63]	1999	Unspecified	HD patients	65	78·5
Zahran, 2014 [64]	–	HD center/units	HD patients	514	49·6
Iran ($n = 41$)					
Aghakhani, 2009 [65]	–	Clinical setting	HD patients	289	3·1
Alavian, 2015 [66]	2012	HD center/units	HD patients	274	0·0
Ali, 2008 [67]	2005–2006	Clinical setting	HD patients	93	24·7
Amiri, 2005 [68]	2001	HD center/units	HD patients	298	24·8
Azarkar, 2009 [69]	2007	Clinical setting	HD patients	30	0·0
Bozorghi, 2006 [70]	2004	Clinical setting	Male HD patients	44	2·3
Bozorghi, 2006 [70]	2004	Clinical setting	Female HD patients	45	8·9
Broumand, 2002 [71]	–	HD center/units	HD patients	548	19·2
Dadgaran, 2005 [72]	–	HD center/units	HD patients	393	17·8
Dadmanesh, 2015 [73]	2012–2013	Clinical setting	HD patients	138	0·0
Eslamifar, 2007 [74]	2006	HD center/units	HD patients	77	6·5
Ghadir, 2009 [75]	2008	HD center/units	HD patients	90	21·1
Haghazali, 2011 [76]	2007	Clinical setting	HD patients	76	7·9

Table 2 (*cont.*)

First author, year of publication	Year(s) of data collection	Study site	Population	Sample size	HCV prev. (%)
Hamissi, 2011 [77]	2009	Clinical setting	Male HD patients	120	5·8
Hamissi, 2011 [77]	2009	Clinical setting	Female HD patients	75	8·0
Jahromi, 2007 [78]	2006	Clinical setting	HD patients	34	5·9
Joukar, 2011 [79]	2009	HD center/units	Female HD patients	228	8·8
Joukar, 2011 [79]	2009	HD center/units	Male HD patients	286	14·3
Kalantari, 2014 [80]	2010	HD center/units	HD patients	499	5·2
Kassaian, 2011 [81]	2009	Clinical setting	HD patients	800	2·1
Mahdavi, 2009 [82]	2005	HD center/units	HD patients	2403	9·4
Mak, 2001 [83]	–	HD center/units	HD patients	86	31·4
Makhlough, 2008 [84]	2006	HD center/units	HD patients	186	11·3
Mansour-Ghanaei, 2009 [85]	2007	Clinical setting	HD patients	163	10·4
Mousavi, 2014 [86]	–	HD center/units	HD patients	47	4·3
Rostami, 2013 [87]	2010–2011	HD center/units	Female HD patients	1704	0·9
Rostami, 2013 [87]	2010–2011	HD center/units	Male HD patients	2259	1·7
Sabur, 2003 [88]	1999–2000	Clinical setting	HD patients	140	26·4
Salehi, 2014 [89]	2008	HD center/units	HD patients	40	10·0
Samarbaf-Zadeh, 2015 [90]	–	HD center/units	HD patients	430	9·1
Samimi-Rad, 2008 [91]	2005	HD center/units	Male HD patients	101	1·0
Samimi-Rad, 2008 [91]	2005	HD center/units	Female HD patients	103	9·7
Seyrafian, 2006 [92]	2005	HD center/units	HD patients	556	2·9
Somi, 2007 [93]	2006	HD center/units	HD patients	462	14·9
Somi, 2014 [94]	2012	HD center/units	HD patients	455	8·1
Taremi, 2005 [95]	2004	HD center/units	HD patients	324	20·4
Taziki, 2008 [96]	2006	HD center/units	HD patients	497	12·3
Taziki, 2008 [96]	2001	HD center/units	HD patients	348	18·4
Toosi, 2007 [97]	–	Clinical setting	HD patients	130	8·5
Zahedi, 2012 [98]	2010	HD center/units	HD patients	228	3·1
Ziaee, 2013 [99]	2010	Clinical setting	HD patients	41	0·0
Iraq ($n = 16$)					
Abdul-Aziz, 2001 [100]	1999–2001	Central laboratory	Male HD patients	62	0·0
Abdul-Aziz, 2001 [100]	1999–2001	Central laboratory	Female HD patients	33	0·0
Abdullah, 2012 [101]	2010	Clinical setting	HD patients	236	38·9
Abdullah, 2012 [102]	2005–2007	Clinical setting	HD patients	80	28·7
Al-Dulaimi, 2012 [103]	2010–2011	Clinical setting	HD patients	84	14·3
Al-Mashhadani, 2006 [104]	2002	Clinical setting	HD patients	87	11·5
Hassan, 2008 [105]	1996–2001	Central laboratory	HD patients	35	14·3
Khattab, 2008 [106]	2003–2005	Clinical setting	Male HD patients	102	4·9
Khattab, 2008 [106]	2003–2005	Clinical setting	Female HD patients	67	10·4
Khattab, 2010 [107]	2003–2008	Clinical setting	Male HD patients	153	3·3
Khattab, 2010 [107]	2003–2008	Clinical setting	Female HD patients	91	7·7
Mnuti, 2011 [108]	2008–2010	Clinical setting	Male HD patients	58	39·6
Mnuti, 2011 [108]	2008–2010	Clinical setting	Female HD patients	42	42·8
Ramzi, 2010 [109]	2009	Clinical setting	Male HD patients	63	25·4
Ramzi, 2010 [109]	2009	Clinical setting	Female HD patients	38	28·9
Shihab, 2014 [110]	2012–2013	Clinical setting	HD patients	122	42·6
Jordan ($n = 9$)					
Al-Jamal, 2009 [111]	2007–2008	Clinical setting	Male HD patients	63	31·7
Al-Jamal, 2009 [111]	2007–2008	Clinical setting	Female HD patients	57	24·5
Batchoun, 2011 [112]	–	Clinical setting	Male HD patients	67	49·2
Batchoun, 2011 [112]	–	Clinical setting	Female HD patients	67	46·3
Batieha, 2007 [113]	2003	National	HD patients	1711	20·5
Bdour, 2002 [114]	–	Clinical setting	HD patients	283	32·5
Ghunaimat, 2007 [115]	–	Clinical setting	Male HD patients	130	43·8
Ghunaimat, 2007 [115]	–	Clinical setting	Female HD patients	79	59·5
Said, 1995 [116]	1994	HD center/units	HD patients	273	24·5

Table 2 (*cont.*)

First author, year of publication	Year(s) of data collection	Study site	Population	Sample size	HCV prev. (%)
Kuwait ($n = 3$)					
Altawalah, 2015 [117]	2012	Clinical setting	Kuwaiti HD patients	740	4·7
Altawalah, 2015 [117]	2012	Clinical setting	Non-Kuwaiti HD patients	625	8·2
El Reshaid, 1995 [118]	1994	Clinical setting	HD patients	232	40·0
Lebanon ($n = 9$)					
Abdelnour, 1997 [119]	–	Clinical setting	HD patients	108	15·7
Abou Rached, 2016 [120]	2010–2012	HD center/units	HD patients in Beirut	559	3·6
Abou Rached, 2016 [120]	2010–2012	HD center/units	HD patients in Mount Lebanon	1632	4·5
Abou Rached, 2016 [120]	2010–2012	HD center/units	HD patients in Beqaa	394	5·6
Abou Rached, 2016 [120]	2010–2012	HD center/units	HD patients in South Lebanon	339	7·1
Abou Rached, 2016 [120]	2010–2012	HD center/units	HD patients in North Lebanon	757	5·0
Abou Rached, 2016 [120]	2010–2012	HD center/units	HD patients in Nabatieh	88	0·0
Mourani, 1999 [121]	1997	Clinical setting	HD patients	20	15·0
Naman, 1996 [122]	–	Clinical setting	HD patients	317	27·0
Libya ($n = 5$)					
Alashek, 2010 [123]	2009	HD center/units	HD patients	749	25·1
Alashek, 2012 [124]	–	HD center/units	HD patients	2410	12·0
Daw, 2002 [125]	1999–2001	–	HD patients	200	20·5
El-Zouki, 1993 [126]	–	Clinical setting	HD patients	47	42·5
Elzouki, 1995 [127]	–	Clinical setting	HD patients	153	21·0
Morocco ($n = 7$)					
Benani, 1997 [128]	–	HD center/units	HD patients	49	48·9
Benjelloun, 1996 [129]	–	HD center/units	HD patients	114	35·1
Boulaajaj, 2005 [130]	1983–2002	Clinical setting	HD patients	186	76·0
Foullous, 2015 [131]	–	HD center/units	HD patients	630	30·8
Lioussfi, 2014 [132]	2009	HD center/units	Patients on peritoneal dialysis	38	8·0
Lioussfi, 2014 [132]	2009	HD center/units	Patients on HD	67	60·0
Sekkat, 2008 [133]	2003–2004	HD center/units	HD patients	303	68·3
Oman ($n = 1$)					
Al-Dhahry, 1992 [134]	1991	Clinical setting	HD patients	102	26·5
Pakistan ($n = 7$)					
Ali, 2011 [135]	–	–	HD patients	25	28·0
Chishti, 2015 [136]	2010–2011	Clinical setting	HD patients	200	29·0
Gul, 2003 [137]	1999	Clinical setting	HD patients	50	68·0
Khan, 2011 [138]	2010	Clinical setting	HD patients	384	29·2
Khokhar, 2005 [139]	2002–2003	Clinical setting	HD patients	97	23·7
Mahmud, 2014 [140]	2012–2013	Mixed setting	HD patients	189	16·4
Mumtaz, 2009 [141]	2008	Clinical setting	HD patients	50	28·0
Palestine ($n = 12$)					
Al Zabadi, 2016 [142]	2014	HD center/units	HD patients in Hebron	177	7·3
Al Zabadi, 2016 [142]	2014	HD center/units	HD patients in Ramallah	135	3·7
Al Zabadi, 2016 [142]	2014	HD center/units	HD patients in Nablus	174	2·9
Al Zabadi, 2016 [142]	2014	HD center/units	HD patients in Beit Jala	93	8·6
Al Zabadi, 2016 [142]	2014	HD center/units	HD patients in Tulkarem	71	5·6
Al Zabadi, 2016 [142]	2014	HD center/units	HD patients in Qalqelia	44	15·9
Al Zabadi, 2016 [142]	2014	HD center/units	HD patients in Jenin	117	15·4
Al Zabadi, 2016 [142]	2014	HD center/units	HD patients in Jericho	25	4·0
Al Zabadi, 2016 [142]	2014	HD center/units	HD patients in Salfeet	32	9·4
Dumaidi, 2014 [143]	2012–2013	Clinical setting	HD patients in Jenin	87	41·4
Dumaidi, 2014 [143]	2012–2013	Clinical setting	HD patients in Tulkarem	59	6·8

Table 2 (*cont.*)

First author, year of publication	Year(s) of data collection	Study site	Population	Sample size	HCV prev. (%)
El-Kader, 2010 [144]	2007	Clinical setting	HD patients	246	17·9
Qatar ($n = 1$)					
Abboud, 1995 [145]	–	Clinical setting	HD patients	130	44·6
Saudi Arabia ($n = 39$)					
Al Ghamdi, 2001 [146]	1997	Clinical setting	HD patients	56	57·0
Al Jiffri, 2003 [147]	1991	Clinical setting	HD patients	248	72·6
Al Mugeiren, 1992 [148]	–	Clinical setting	HD patients	20	45·0
Al Muhanna, 1995 [149]	–	Clinical setting	HD patients	162	43·2
Al Nasser, 1992 [150]	–	Clinical setting	Male HD patients	40	42·5
Al Nasser, 1992 [150]	–	Clinical setting	Female HD patients	26	50·0
Al Saran, 2014 [151]	2009	Clinical setting	HD patients	144	27·8
Al Shohaib, 1995 [152]	1992	Clinical setting	HD patients	139	52·5
Alsaran, 2009 [153]	2007–2008	Clinical setting	HD patients	83	33·0
Ayoola, 1991 [154]	–	Clinical setting	Male HD patients	33	42·5
Ayoola, 1991 [154]	–	Clinical setting	Female HD patients	41	41·5
Bahakim, 1991 [155]	1990	Clinical setting	HD patients	65	26·1
Bernieh, 1995 [156]	1991	Clinical setting	HD patients	94	60·0
Fakunle, 1991 [157]	–	Clinical setting	Nationals HD patients	113	48·7
Fakunle, 1991 [157]	–	Clinical setting	Expatriates HD patients	77	61·0
Huraib, 1995 [158]	–	HD center/units	HD patients	1147	68·0
Hussein, 1994 [159]	1993	Clinical setting	HD patients	67	40·0
Hussein, 2007 [160]	2003	Clinical setting	HD patients	180	18·9
Karkar, 2006 [161]	–	Clinical setting	HD patients	265	29·0
Kashem, 2002 [162]	–	Clinical setting	HD patients	75	46·0
Kashem, 2003 [163]	2002	Clinical setting	HD patients	90	46·7
Kumar, 1997 [164]	1993–1996	Clinical setting	HD patients	47	51·1
Mitwalli, 1992 [165]	–	Clinical setting	HD patients	36	22·2
Mitwalli, 2000 [166]	1997	Clinical setting	HD patients	109	54·1
Saran, 2011 [167]	2009	Clinical setting	HD patients	146	24·1
Saxena, 2001 [168]	–	Clinical setting	HD patients	189	43·9
Saxena, 2003 [169]	1995–2000	Clinical setting	Male HD patients	99	49·5
Saxena, 2003 [169]	1995–2000	Clinical setting	Female HD patients	97	33·0
Saxena, 2003 [170]	1995–2000	Clinical setting	Male HD patients	91	38·5
Saxena, 2003 [170]	1995–2000	Clinical setting	Female HD patients	98	49·0
Saxena, 2004 [171]	1995–2000	Clinical setting	Male HD patients	86	62·8
Saxena, 2004 [171]	1995–2000	Clinical setting	Female HD patients	86	37·2
Shaheen, 1995 [172]	–	Clinical setting	HD patients	408	72·3
Shobokshi, 2003 [173]	1998–2002	Clinical setting	HD patients	29 054	55·7
Souqiyyeh, 1995 [174]	1993–1994	Clinical setting	HD patients	1392	54·0
Souqiyyeh, 2001 [175]	2000	HD center/units	HD patients	6694	50·0
Soyannwo, 1996 [176]	1992	Clinical setting	Male HD patients	47	53·2
Soyannwo, 1996 [176]	1992	Clinical setting	Female HD patients	49	46·9
Tashkandy, 2012 [177]	2000–2004	Clinical setting	HD patients	1357	78·2
Sudan ($n = 3$)					
El-Amin, 2007 [178]	2005	HD center/units	HD patients	236	23·7
Gasim, 2012 [179]	2010	HD center/units	HD patients	353	8·5
Suliman, 1995 [180]	1994	HD center/units	HD patients	46	34·9
Syria ($n = 5$)					
Abdulkarim, 1998 [181]	–	HD center/units	HD patients	120	75·0
Othman, 2001 [182]	1996	Clinical setting	Male HD patients	80	53·7
Othman, 2001 [182]	1996	Clinical setting	Female HD patients	59	42·4
Moukeh, 2009 [183]	2006	Clinical setting	Male HD patients	280	53·9
Moukeh, 2009 [183]	2006	Clinical setting	Female HD patients	270	54·8
Tunisia ($n = 14$)					
Ayed, 2003 [184]	2001	HD center/units	HD patients in Tunis	1394	22·2

Table 2 (*cont.*)

First author, year of publication	Year(s) of data collection	Study site	Population	Sample size	HCV prev. (%)
Ayed, 2003 [184]	2001	HD center/units	HD patients in the Northwestern region	358	15·4
Ayed, 2003 [184]	2001	HD center/units	HD patients in the Northern region	279	15·7
Ayed, 2003 [184]	2001	HD center/units	HD patients in the Northeastern region	199	30·1
Ayed, 2003 [184]	2001	HD center/units	HD patients in the central region	1314	18·5
Ayed, 2003 [184]	2001	HD center/units	HD patients in the Southern region	796	14·6
Ben Othman, 2004 [185]	2000–2002	HD center/units	HD patients in Sousse	143	29·4
Ben Othman, 2004 [185]	2000–2002	HD center/units	HD patients in Monastir	47	31·9
Ben Othman, 2004 [185]	2000–2002	HD center/units	HD patients in Mahdia	86	38·4
Hmaied, 2006 [186]	2001–2003	HD center/units	HD patients	395	20·0
Hachicha, 1995 [187]	–	HD center/units	HD patients	235	36·6
Hmida, 1995 [188]	–	HD center/units	HD patients	235	45·1
Jemni, 1994 [189]	–	HD center/units	HD patients	63	42·0
Sassi, 2000 [190]	–	HD center/units	HD patients	58	46·5
United Arab Emirates ($n = 1$)					
El Shahat, 1995 [191]	1991–1993	Clinical setting	HD patients	262	24·0
Yemen ($n = 3$)					
Aman, 2015 [192]	2000–2013	HD center/units	HD patients	219	40·2
Haidar, 2002 [193]	1997–1999	Clinical setting	HD patients	30	40·0
Selm, 2010 [194]	2007	Clinical setting	HD patients	51	62·7

HD, Hemodialysis; Prev., Prevalence.

< 0·1 for all three variables). Sample size was not associated with HCV prevalence (*P*-value > 0·7).

In the final multivariable analysis, region and year of data collection were included, but income group was not due to collinearity. The model explained 54·48% of the variation. Relative to the Fertile Crescent, the odds (for higher HCV prevalence) was much larger in Egypt; adjusted odds ratio (AOR) of 7·43 (95% CI: 4·44–12·44). It was also higher in Pakistan (AOR = 2·47; 95% CI: 1·07–5·69) and the Gulf region (AOR = 1·77; 95% CI: 1·08–2·90), but lower in Iran (AOR = 0·38; 95% CI: 0·24–0·58). Importantly, the AOR for the year of data collection was 0·92 (95% CI: 0·90–0·95) indicating declining HCV prevalence in HD patients year by year.

Risk factors for HCV infection among HD patients

Few studies assessed risk factors for HCV infection among HD patients. Duration and frequency of dialysis and exposure to blood transfusions were the most commonly reported risk factors [45, 51, 52, 62, 109, 182].

HCV genotype and subtype distribution among HD patients

Table 6 shows the frequency, distribution, and Shannon Diversity Index of HCV genotypes among HD patients. Supplementary Fig. S2 also shows the distribution of HCV genotypes and subtypes.

The vast majority (92·3%) of viremic HD patients were infected by a single strain (Supplementary Fig. S2). At the regional level, four HCV genotypes were documented in HD patients: genotype 1 (68·8%), genotype 2 (9·6%), genotype 3 (7·9%), and genotype 4 (13·5%). Weighted by country population size, the regional genotype distribution was: genotype 1 (39·3%), genotype 2 (5·7%), genotype 3 (29·6%), and genotype 4 (25·4%). No cases of genotypes 5, 6, and 7 were reported.

Genotype 1 was commonly found in Morocco (100%), Tunisia (77·3%), Jordan (73·3%), Syria (60·7%), Iran (55·7%), Bahrain (55·5%), Iraq (51·5%), and Saudi Arabia (46·8%). It was also common in Lebanon (28·1%), Pakistan (22·2%), and Egypt (16·1%).

Table 3. *Pooled mean estimate for hepatitis C virus (HCV) antibody prevalence among hemodialysis patients across countries of the Middle East and North Africa*

	Studies	Samples	HCV Prevalence across studies		Pooled HCV prevalence		Heterogeneity measures		
Country	Total *N*	Total *N*	Range (%)	Median	Mean (%)	95% CI	Q^a (*P*-value)	I^{2b} (95% CI)	Prediction interval[c] (%)
Algeria	3	4101	22·8–42·0	23·8	29·3	17·4–42·7	133·7 ($P < 0·0001$)	98·5 (97·4–99·1)	0·0–100
Egypt	26	4915	10·0–100	69·0	65·5	56·5–74·1	809·1 ($P < 0·0001$)	96·9 (96·2–97·5)	18·9–98·6
Iran	41	15 140	0–31·4	8·5	9·2	5·9–10·8	1076·5 ($P < 0·0001$)	96·3 (95·6–96·9)	0·0–29·4
Iraq	16	1353	0–42·9	14·3	16·6	9·0–25·7	248·2 ($P < 0·0001$)	94·0 (91·6–95·6)	0·0–62·1
Jordan	9	2730	20·5–59·5	32·5	36·1	27·4–45·2	120·7 ($P < 0·0001$)	93·4 (89·5–95·8)	9·0–69·1
Kuwait	3	1597	4·7–40·0	8·2	14·9	2·8–34·1	155·8 ($P < 0·0001$)	98·7 (97·8–99·2)	0·0–100
Lebanon	9	4214	0–27·0	5·6	7·3	3·7–11·7	159·0 ($P < 0·0001$)	95·0 (92·3–96·7)	0·0–27·1
Libya	5	3559	12·0–42·5	21·0	22·5	14·2–31·9	95·1 ($P < 0·0001$)	95·8 (92·7–97·6)	0·6–61·2
Morocco	7	1387	8·0–76·0	49·0	46·4	28·5–64·7	239·4 ($P < 0·0001$)	97·5 (96·3–98·3)	0·2–98·1
Pakistan	7	995	16·4–68·0	28·0	30·4	21·7–39·9	49·4 ($P < 0·0001$)	87·8 (77·3–93·5)	5·7–63·5
Palestine	12	1260	2·9–41·4	8·0	10·3	5·6–16·2	93·8 ($P < 0·0001$)	88·3 (81·4–92·6)	0·0–36·8
Saudi Arabia	39	43 250	18·9–78·2	46·9	47·4	43·7–51·1	998·1 ($P < 0·0001$)	96·2 (95·5–96·8)	26·8–68·4
Sudan	3	635	8·5–34·9	23·7	20·4	7·6–37·2	36·4 ($P < 0·0001$)	94·5 (87·3–97·6)	0·0–100
Syria	5	809	42·4–75·0	53·9	56·6	47·5–65·5	24·2 ($P < 0·0001$)	83·5 (62·6–92·7)	24·7–85·7
Tunisia	14	5602	14·6–46·5	29·8	27·4	22·6–32·5	194·4 ($P < 0·0001$)	93·3 (90·4–95·3)	10·3–48·9
Yemen	3	300	40·0–62·7	40·2	47·4	32·7–62·3	8·6 ($P = 0·010$)	76·8 (24·2–92·9)	0·0–100
Oman	1	102	–	–	26·5	18·2–36·1	–	–	–
Qatar	1	130	–	–	44·6	35·9–53·6	–	–	–
UAE	1	262	–	–	24·4	19·3–30·1	–	–	–
Pooled HCV prevalence stratified by temporal duration									
1989–1998	50	8964	15·7–100	46·5	51·6	46·1–57·1	1235·3 ($P < 0·0001$)	96·0 (95·4–96·6)	16·0–86·3
1999–2008	69	53 500	0·0–78·5	23·8	27·8	23·1–32·8	7325·6 ($P < 0·0001$)	99·1 (99·0–99·1)	0·8–71·6
2009–2016	86	29 877	0·0–94·1	9·7	18·8	14·5–23·5	7941·1 ($P < 0·0001$)	98·9 (98·8–99·0)	0·0–68·8
All countries	205	92 341	0–100	26·5	29·2	25·6–32·8	26 145·8 ($P < 0·0001$)	99·2 (99·2–99·3)	0·0–82·0

CI, Confidence interval; UAE, United Arab Emirates.

[a] *Q*: The Cochran's *Q* statistic is a measure assessing the existence of heterogeneity in effect size.

[b] I^2: A measure that assesses the magnitude of between-study variation that is due to differences in effect size across studies rather than chance.

[c] Prediction interval: A measure that estimates the 95% interval in which the true effect size in a new study will lie.

Table 4. *Pooled mean estimate for hepatitis C virus (HCV) viremic rate among hemodialysis patients across countries of the Middle East and North Africa. HCV viremic rate is the prevalence of HCV chronic infection (HCV RNA positivity) among antibody-positive persons*

Country	Studies Total *N*	Samples Total *N*	HCV RNA prevalence among antibody positive persons		Pooled HCV viremic rate		Heterogeneity measures		
			Range (%)	Median	Mean (%)	95% CI	Q^a (*P*-value)	I^{2b} (95% CI)	Prediction interval[c] (%)
Iran	4	219	48·6–64·3	52·3	51·1	44·3–57·9	1·3 ($P = 0·7$)	0·0 (0·0–65·0)	36·4–68·8
Iraq	2	144	26·1–61·5	43·8	38·9	30·9–47·4	–	–	–
Jordan	1	92	–	–	31·5	22·2–42·0	–	–	–
Lebanon	2	63	30·4–65·0	47·7	39·7	27·6–52·8	–	–	–
Libya	1	32	–	–	72·0	53·2–86·2	–	–	–
Morocco	4	309	48·9–70·0	59·7	57·9	49·2–66·5	5·3 ($P = 0·1$)	43·5 (0·0–81·1)	27·0–85·9
Pakistan	1	25	–	–	28·0	12·1–49·4	–	–	–
Palestine	2	290	19·1–84·1	51·6	29·0	28·8–34·5	–	–	–
Syria	1	56	–	–	87·5	75·9–94·8	–	–	–
Tunisia	13	1942	51·0–93·3	76·2	75·1	69·6–80·2	61·9 ($P < 0·0001$)	80·6 (67·8–88·3)	54·6–91·1
All countries	31	3172	19·1–93·3	65·4	63·0	55·4–70·3	499·9 ($P < 0·0001$)	94·0 (92·4–95·2)	21·7–95·5

HCV, Hepatitis C virus; RNA, Ribonucleic acid.

[a] *Q*: The Cochran's Q statistic is a measure assessing the existence of heterogeneity in effect size.

[b] I^2: A measure that assesses the magnitude of between-study variation that is due to differences in effect size across studies rather than chance.

[c] Prediction interval: A measure that estimates the 95% interval in which the true effect size in a new study will lie.

Table 5. *Univariable and multivariable meta-regression models for hepatitis C virus (HCV) antibody prevalence among hemodialysis patients across the Middle East and North Africa*

		Univariable analysis		Multivariable analysis[a]	
	Number of studies	OR (95% CI)	*P*-value	AOR (95% CI)	*P*-value
Region					
Fertile Crescent[b]	51	1·0	–	1·0	–
Egypt	26	11·15 (6·49–19·16)	0·000	7·43 (4·44–12·44)	0·000
Gulf[c]	45	3·85 (2·43–6·10)	0·000	1·77 (1·08–2·90)	0·022
Horn of Africa[d]	6	2·48 (0·94–6·55)	0·065	1·82 (0·74–4·46)	0·189
Iran	41	0·37 (0·23–0·59)	0·000	0·38 (0·24–0·58)	0·000
Maghreb[e]	29	2·30 (1·36–3·88)	0·002	1·47 (0·89–2·43)	0·130
Pakistan	7	2·32 (0·93–5·74)	0·068	2·47 (1·07–5·69)	0·033
Income group[f]					
LMIC	65	1·0	–	–	–
UMIC	95	0·12 (0·08–0·18)	0·000	–	–
HIC	45	0·78 (0·49–1·24)	0·303	–	–
Year of data collection	205	0·89 (0·87–0·91)	0·000	0·92 (0·90–0·95)	0·000
Sample size	205	1·00 (0·99–1·00)	0·677	–	–

OR, Odds ratio; AOR, Adjusted odds ratio; LMIC, Low middle-income country; UMCI, Upper middle-income country; HIC, High-income country.
[a] The adjusted R-square for the full model was 54·48%.
[b] Fertile Crescent includes: Iraq, Jordan, Lebanon, Palestine, and Syria.
[c] Gulf includes: Kuwait, Oman, Qatar, Saudi Arabia, and Unite Arab Emirates.
[d] Horn of Africa includes: Yemen and Sudan.
[e] Maghreb includes: Algeria, Libya, Morocco, and Tunisia.
[f] Income group was removed from the multivariable analysis because of collinearity.

Genotype 4 was commonly found in Egypt (83·9%), Saudi Arabia (50·0%), Iraq (45·4%), and Lebanon (40·6%). It was also present in the rest of the countries apart from Morocco. Pakistan was the only country where genotype 3 was the most common genotype (62·2%). Genotype 3 was also common in Iran (39·4%), but otherwise rare in the rest of the countries. Genotype 2 was common in Bahrain (33·3%) and Lebanon (25·0%), and somewhat common in Pakistan (13·3%) and Tunisia (11·8%), but otherwise rare.

For genotype 1, subtype 1a and 1b were commonly observed in MENA (Supplementary Fig. S2). Subtypes 2a, 2b, 2c, 3a, 3b, and 4a were also detected in this region. Combinations of the above genotypes and subtypes were observed among multiply infected individuals.

Genotype diversity varied across countries. It was highest in Lebanon with a relative Shannon Diversity Index of 63·7% (score: 1·24 out of a maximum of 1·95) and lowest in Morocco 0·0% (score: 0·0 out of a maximum of 1·95). For the region as a whole, the relative Shannon Diversity Index was 49·1% (score: 0·95 out of a maximum of 1·95) for the unweighted analysis, and 63·9% (score: 1·24 out of a maximum of 1·95) for the weighted analysis by country population size.

DISCUSSION

Through a comprehensive investigation of HCV epidemiology among HD patients in MENA, we found that there is ongoing and considerably high HCV incidence in this population across the region. However, the incidence rate varied between countries and across different settings within the same country (Supplementary Table S2). We also found high HCV prevalence in HD patients, with the prevalence varying substantially across the region and within each country. About one-third (29·2%) of HD patients have already been infected with HCV (Table 3), with two-thirds of them (63·0%) being chronic carriers (Table 4) that can potentially transmit the infection to other patients through dialysis. We also found substantial diversity of HCV genotypes in HD patients, with genotype 1 being the most common at the regional level (Table 6). Importantly, we found that HCV prevalence in HD patients is on a declining trend (Tables 3 and 5).

Table 6. *Frequency, distribution, and Shannon Diversity Index of hepatitis C virus (HCV) genotypes among hemodialysis patients across the Middle East and North Africa*

Country	Studies Total *N*	Samples Total *N*	Genotype 1 *n* (%)	Genotype 2 *n* (%)	Genotype 3 *n* (%)	Genotype 4 *n* (%)	Shannon diversity index (*H*)[a]	Index relative to total possible diversity
Bahrain	1	9	5 (55·5%)	3 (33·3%)	–	1 (11·1%)	0·94	48·1%
Egypt	1	62	10 (16·1%)	–	–	52 (83·9%)	0·44	22·7%
Iran	7	269	150 (55·7%)	–	106 (39·4%)	13 (4·8%)	0·84	43·1%
Iraq	2	33	17 (51·5%)	–	1 (3%)	15 (45·4%)	0·81	41·6%
Jordan	1	30	22 (73·3%)	–	–	8 (26·6%)	0·58	29·8%
Lebanon	4	64	18 (28·1%)	16 (25%)	4 (6·2%)	26 (40·6%)	1·24	63·7%
Morocco	2	68	68 (100%)	–	–	–	0·00	0·0%
Pakistan	1	90	20 (22·2%)	12 (13·3%)	56 (62·2%)	2 (2·2%)	0·98	50·5%
Saudi Arabia	1	32	15 (46·8%)	1 (3·1%)	–	16 (50·0%)	0·81	41·6%
Syria	1	28	17 (60·7%)	–	–	11 (39·3%)	0·67	34·4%
Tunisia	10	1529	1182 (77·3%)	181 (11·8%)	10 (1%)	156 (10·0%)	0·72	36·8%
All countries (unweighted)	31	2214[b]	1524 (68·8%)	213 (9·6%)	177 (7·9%)	300 (13·5%)	0·95	49·1%
All countries (weighted by population size)	31	2214[b]	1524 (39·3%)	213 (5·7%)	177 (29·6%)	300 (25·4%)	1·24	63·9%

No data were found for HCV genotypes 5, 6, and 7.

[a] The maximum value for Shannon Diversity Index is 1·95 assuming full genotype diversity of seven HCV genotypes [17, 37].

[b] Each individual testing positive for multiple genotypes contributed separately to the sum of cases for each genotype.

These findings suggest that the standard of infection control in dialysis differs across countries and across dialysis units within each country. They also indicate that extensive improvement is needed to control HCV transmission among HD patients. Fortunately, improvements appear to be already taking place as validated by the declining trend in prevalence. These findings highlight further the importance of addressing HCV infection and disease burden in HD patients, especially considering the recent availability and increasing affordability of DAAs for HCV treatment [4], and that the number of patients undergoing dialysis is rising rapidly with the aging of the population and growing prevalence of chronic diseases that lead to renal disease [40, 195–197].

Our pooled mean estimate for HCV prevalence indicated that HCV prevalence among HD patients in MENA is higher than that in other regions such as Europe (7·2%) [198], the USA (7·9%) [199, 200], and the Asia-Pacific region (range across countries of 1–18%) [201]. This finding may not only suggest inferior standards of dialysis in MENA, but may also reflect the higher background HCV prevalence in the whole population in this region [2, 3]. Indeed, HCV prevalence among HD patients in MENA countries reflected in part HCV prevalence in the population at large in each country. For example, HCV prevalence among HD patients in Egypt and Pakistan was much higher than that in other MENA countries (Table 5), reflecting the higher prevalence in the wider population in these two countries [13, 22].

The high HCV incidence and prevalence in HD patients appear to reflect improper application of infection control measures, such as by healthcare personnel to maintain hands hygiene [199, 202], to change gloves routinely [199, 202], and to clean the dialysis unit and equipment properly between patients [8, 203]. With the continuing conflict emergencies in several countries and the large refugee and migrant populations, overloading dialysis units and depletion of medical resources is a growing concern [204, 205]. These emergencies appear to have led to reuse and sharing of supplies and equipment intended for single usage such as infusion vials and machine filters [205, 206]. The lingering emergencies may undermine the recent improvements and reverse the trend of declining HCV prevalence in HD patients.

We found substantial diversity in the circulating HCV genotypes in HD patients across countries. However, this diversity appeared to reflect the distribution of circulating genotypes in each country

[207]. For example, the dominant genotypes among HD patients in Egypt and Pakistan were genotypes 4 and 3, respectively (Table 6), similar to the dominant genotypes in the wider population in these two countries [207]. These findings may indicate overlapping transmission networks where HCV is circulating from one population to another through different modes of exposure including dialysis.

A review of HCV among HD patients in the Middle East has been recently published [208]. Its findings agreed overall with our findings despite differences between the two studies in the focus, scope, and analysis plans. Our study covered more countries in MENA over a longer duration, examined analytically trends and associations, and reported a broader set of outcome measures and analyses (such as for the genotype distribution). In total, 205 studies were included in our analyses compared to 56 studies in Ashkani-Esfahani *et al.* study [208]. Both studies concluded that there is high HCV prevalence in HD patients that needs to be addressed through targeted interventions.

Our study had several limitations. The availability of data varied from one county to another and we did not identify any data for five MENA countries (Afghanistan, Bahrain, Djibouti, Mauritania, and Somalia). Sample size varied also across studies and the sampled HD populations may have been sampled from specific geographic areas within a given country, and may not be representative of the wider HD population in the country. Despite these limitations, we were able to identify a large volume of data for MENA countries that allowed us to conduct different types of analyses, generate multiple inferences, and produce a comprehensive mapping of HCV epidemiology among HD patients in this region.

CONCLUSIONS

Our findings revealed ongoing HCV incidence and high HCV prevalence among HD patients in MENA, but incidence and prevalence appear to be declining year by year. About one-fifth of HD patients are chronic carriers of HCV infection, in need of HCV treatment, and potentially can transmit the infection to other HD patients. In context of rapidly growing HD patient population, these findings highlight the need to improve standards of infection control in dialysis in MENA.

Moreover, in context of recent availability and increasing affordability of DAAs for HCV treatment, these findings highlight the urgency to address HCV infection and disease burden in HD patients. Governments that are reluctant to take on national level HCV elimination projects, could initially focus on HD patients as a candidate population for micro-elimination as a way to advance the agenda for HCV DAA treatment. With HCV circulation among HD patients being a major mode of HCV transmission, tackling this infection and disease burden is critical to HCV global elimination and mortality reduction targets by 2030.

SUPPLEMENTARY MATERIAL

The supplementary material for this article can be found at https://doi.org/10.1017/S0950268817002242.

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DECLARATION OF INTEREST

The authors have no competing interest to declare.

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