



Review

Epidemiology of hepatitis C virus in the Arabian Gulf countries: Systematic review and meta-analysis of prevalence



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SUMMARY

Objective: The aims of this study were to perform a systematic review and synthesize epidemiological data on hepatitis C virus (HCV) in the Arabian Gulf countries, and to assess the country-specific prevalence among nationals and expatriate populations.

Methods: A systematic review of HCV antibody prevalence and incidence in the Arabian Gulf countries was conducted, based on the items outlined in the PRISMA statement. Meta-analyses were performed incorporating inverse variance weighting and using a random-effects model to pool summary estimates of HCV prevalence among general population groups, for nationals and the entire resident population.

Results: A total of 557 prevalence measures and one incidence measure were identified for the Arabian Gulf countries. HCV prevalence among nationals was 0.24% (95% confidence interval (CI) 0.02–0.63) in the United Arab Emirates (UAE), 0.44% (95% CI 0.29–0.62) in Kuwait, 0.51% (95% CI 0.43–0.59) in Qatar, and 1.65% (95% CI 1.40–1.91) in Saudi Arabia. No data were available for Bahrain or Oman. Among the entire resident populations, HCV prevalence was 0.30% (95% CI 0.23–0.38) in Bahrain, 0.41% (95% CI 0.35–0.46) in Oman, 1.06% (95% CI 0.51–1.81) in Qatar, 1.45% (95% CI 0.75–2.34) in Kuwait, 1.63% (95% CI 1.42–1.84) in Saudi Arabia, and 1.64% (95% CI 0.96–2.49) in UAE. A higher prevalence was observed among expatriate populations such as Egyptians. Among the high-risk populations, HCV prevalence was as high as 78.6% in the multi-transfused and 74.6% in people who inject drugs.

Conclusions: National-level HCV prevalence in the Arabian Gulf region is comparable to global levels. A higher prevalence is found in specific expatriate populations, reflecting the prevalence in their countries of origin. Most exposures appear to occur in high-risk groups and these are often linked to medical care.

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1. Introduction

The Middle East and North Africa (MENA) region appears to have the highest prevalence of hepatitis C virus (HCV) infection worldwide.^{1,2} A few countries in the region are heavily affected by HCV, including Egypt with a prevalence of 14.7%^{3,4} and Pakistan with a prevalence of 4.8%.⁵ The scale of the infection burden in the Arabian Gulf countries remains poorly understood.

Geographically, the Arabian Gulf region encompasses six countries: Bahrain, Kuwait, Oman, Qatar, Saudi Arabia, and the United Arab Emirates (UAE). These countries share common socio-cultural values and economic attributes, and together constitute

the Gulf Cooperation Council (GCC), a political and economic union established in 1981.⁶ Public health policy and programs are often designed and implemented at the level of the GCC. GCC countries are marked by the diversity of their resident populations and exhibit one of the highest ratios of migrants to nationals in the world. More than half of the regional population is expatriate (55.9%).⁷ In Kuwait, Qatar, and UAE, non-nationals comprise more than three-fourths of the population.⁷

The aim of this study was to characterize the epidemiology of HCV in the Arabian Gulf by delineating HCV prevalence among the different risk groups in each of the six countries and by estimating the country-specific HCV population-level prevalence among nationals as well as the entire resident population of nationals and expatriates. The study was conducted under the umbrella of the MENA HCV Epidemiology Synthesis Project, an ongoing effort to characterize the epidemiology of HCV in the MENA region.^{4,8–10}

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The goal of this project is to provide the empirical evidence necessary for policy-makers and public health stakeholders to set the key research, policy, and programming priorities for the MENA region.

2. Methods

The study methodology was developed based on an adaptation of a recently published protocol for conducting systematic reviews and meta-analyses of HCV in the Horn of Africa subregion of MENA.^{9,11} The main features of this methodology are described below.

2.1. Data sources and search strategy

The systematic review was conducted on the basis of the items outlined in the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines.¹² The study objective was to assess HCV antibody prevalence (seroprevalence) and incidence (seroincidence) in the different population groups in the six countries of the Gulf Region: Bahrain, Kuwait, Oman, Qatar, Saudi Arabia, and UAE.¹³ The PRISMA checklist can be found in the **Supplementary Material** (SM 1). The main data sources were the PubMed and Embase databases (accessed February 2, 2015), which were searched using both MeSH/Emtree terms and text terms, with no time or language restrictions. MeSH/Emtree terms were exploded to cover all subheadings. Details of the search criteria for each of these databases can be found in the **Supplementary Material** (SM 2). Additional sources of data were primarily obtained through the MENA HIV/AIDS Epidemiology Synthesis Project database.^{14,15} These included the gray literature, such as country-level reports.

2.2. Study selection

Search results were imported into the reference manager, Endnote, where duplicate publications were identified and excluded. The titles and abstracts of all records retrieved were screened for relevance independently by two of the authors (YM and SR). This involved screening all titles and abstracts to exclude all non-relevant articles. The full texts of all articles deemed relevant or potentially relevant after the initial screening were then retrieved and screened. Inconsistencies between reviewers were discussed and resolved by consensus.

A publication was considered eligible for inclusion in the review if it was conducted in any of the six countries included and had data on at least one of the following outcomes of interest: (1) prevalence of HCV as detected by HCV antibodies, and (2) incidence of HCV as detected by HCV antibodies. Only studies reporting primary data were included. Reviews of the literature were excluded, but all data reported in them were checked and compared to the present search results. Any additional study identified in reviews and not retrieved by the present search was added. Editorials, case notifications, and case series were excluded. All other study designs were eligible for inclusion. A distinction was made between the number of reports (published documents, i.e., papers, conference abstracts, or country-level reports) and the number of outcomes. A report could contribute more than one outcome measure. Outcomes in more than one population/setting within a report were included separately. Outcomes duplicated in more than one report were included only once. Results were synthesized into one list containing all eligible unique outcome measures.

2.3. Data extraction and population classification

The following data were then extracted from each relevant report included in the review: reference details (author, title,

journal, year of publication), country, city/region, study design, sampling technique, study population, socio-demographic characteristics of the population, sample size, number of individuals tested for HCV (if different from the sample size), number of individuals who tested positive, and the reported prevalence and incidence of HCV. Data on HCV RNA prevalence among study population(s) were also extracted from relevant studies whenever available.

Extracted data were then classified and analyzed on the basis of the study population's risk of acquiring HCV. The four defined major population risk groups are the following: (1) populations at high risk,^{4,8} including multi-transfused patients such as thalassemics, hemodialysis patients, and people who inject drugs (PWID), among others; (2) populations at intermediate risk,^{4,8} including familial contacts to HCV patients (i.e., their children, spouses, and other household contacts), select practitioners of professions at risk of HCV (such as healthcare workers (HCWs) and medical students), and populations with health facility/injecting exposures (such as diabetic patients and hospitalized populations); (3) general population groups (populations at low risk of HCV exposure),^{4,8} including pregnant women, blood donors, children, college students, individuals undergoing pre-marital blood screening, expatriate workers undergoing mandatory pre-employment screening, outpatient clinic attendees, and other general population groups (such as populations defined in studies as simply healthy populations, or healthy organ donors); and (4) special clinical population groups,^{4,8} such as hepatocellular carcinoma patients (HCC), viral hepatitis patients, lichen planus patients, schistosomiasis patients, and chronic liver disease (CLD) patients, among others. This final category includes patients with specific diseases that are associated with HCV infection, or patients requiring clinical attention and who could thus be exposed to HCV at medical care facilities, but at variable levels of exposure risk that are difficult to categorize into any of the other population groups mentioned.

2.4. Quantitative analysis

Analyses were conducted using R3.0.1 and Stata/SEv13. The DerSimonian–Laird random-effects method was used to pool study estimates.¹⁶ This method assumes that the true effect size is normally distributed and could vary from one study to another,¹⁷ thus accounting for both sampling variation and heterogeneity in effect size. Effect sizes of individual measures were weighted by their inverse variance. The variance was stabilized using the Freeman–Tukey type arcsine square-root transformation.¹⁸ Back-transformed pooled proportions were then calculated using Miller's inverse transformation with the harmonic mean of the sample sizes.¹⁹ The I^2 value and its confidence interval (CI) were calculated to examine the magnitude of the variation between measures due to heterogeneity rather than chance.²⁰ A two-sided probability value of <0.10 was considered as significant.⁹

As a main objective was to estimate the country-specific HCV population-level prevalence in each of the six countries for which sufficient data were available, only HCV prevalence measures of general population groups were included in this analysis. The prevalence measures were stratified by country and then stratified further into prevalence measures among nationals only and measures including the entire resident populations, i.e. both nationals and expatriates. Stratification by expatriates only could not be done since few reports provided this information. For outcome measures missing either the number of individuals tested for HCV antibodies (denominator) or the number of individuals testing anti-HCV positive (numerator), but reporting HCV prevalence, missing values were calculated using the available information. The 95% CI were estimated for each pooled mean prevalence.

For the overall resident population samples, every available prevalence measure was included whether nationality was stated, unstated, or a mixture of nationalities was implied. In the absence of stratification in a study sample, the overall outcome measure was included. For reports with both stratifications and overall measures, for example overall prevalence in the sample and also prevalence stratified by sex and prevalence stratified by year, the prevalence stratified by sex was selected for inclusion because of the greater epidemiological relevance. In doing so the other two measures (overall and by year) were excluded to avoid bias arising from the duplication of measures from the same population.

Since there was a large number of reported HCV prevalences for Saudi Arabia, a meta-analysis was conducted to estimate HCV prevalence in the different geographic regions of this country. This analysis included only reports in which the city or region information was available. Reports with information on cities and not regions were classified into their respective regions as defined by Al-Faleh et al.²¹

3. Results

3.1. Search results

A schematic diagram of the study selection process can be seen in Figure 1, as adapted from the PRISMA 2009 flow diagram.¹² A total 723 records were identified (321 through PubMed and 402 through Embase) as of February 2, 2015. Of these records, 254 were excluded as duplicates. On assessing all documents for eligibility, the full texts of 199 records were identified for full-text screening, in addition to two records identified through the

references of reviews and four country-level reports identified through the MENA HIV/AIDS Synthesis Project database. Of these records, 159 reports were found to be relevant and were included in this study.

3.2. HCV prevalence overview

Data on HCV prevalence as well as other indicators were abstracted from the 159 relevant reports. Details of all outcome measures are given in the **Supplementary Material** (tables SM 3–6). In total, 556 prevalence measures were identified in this study. Most measures presenting HCV prevalence in the region were from Saudi Arabia ($n = 442$), followed by Kuwait ($n = 43$), UAE ($n = 30$), Qatar ($n = 23$), Oman ($n = 12$), and Bahrain ($n = 6$). The populations studied ranged from general population groups ($n = 335$), to high-risk groups ($n = 112$), intermediate-risk groups ($n = 47$), and special clinical populations ($n = 61$). The majority of studies followed a cross-sectional design (90%) and relied on convenience sampling (93%). Study sample sizes and sex distributions varied.

3.2.1. Bahrain

Three reports indicated HCV prevalence in Bahrain among high-risk populations or special clinical populations (Figure 2B; **Supplementary Material** 7B). HCV prevalence among hemodialysis patients was between 7.4% and 9.24%. A study by Al-Mahroos and Ebrahim published in 1995, conducted among children with hemolytic anemia, found HCV prevalence to be 40% among children who had undergone at least one transfusion and 2% among those with no history of transfusion.²² Two studies were conducted in general population groups (Figure 3B). Both studies

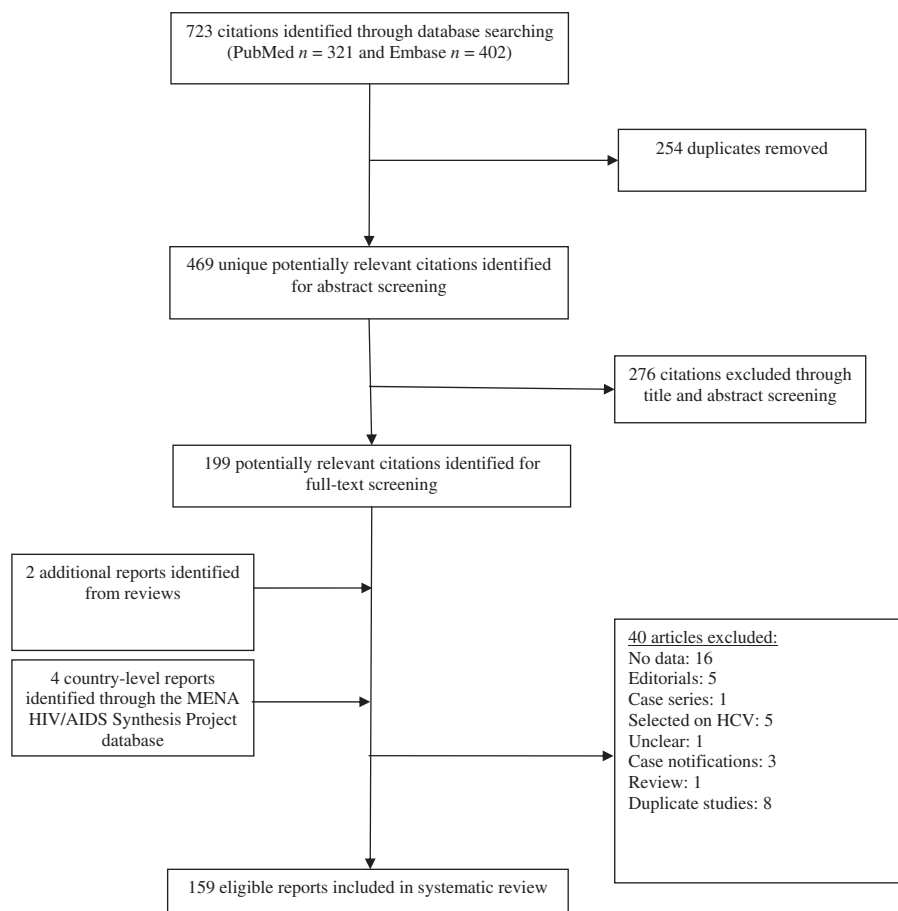


Figure 1. Flow of article selection for the hepatitis C virus (HCV) prevalence and incidence in the Arabian Gulf search.

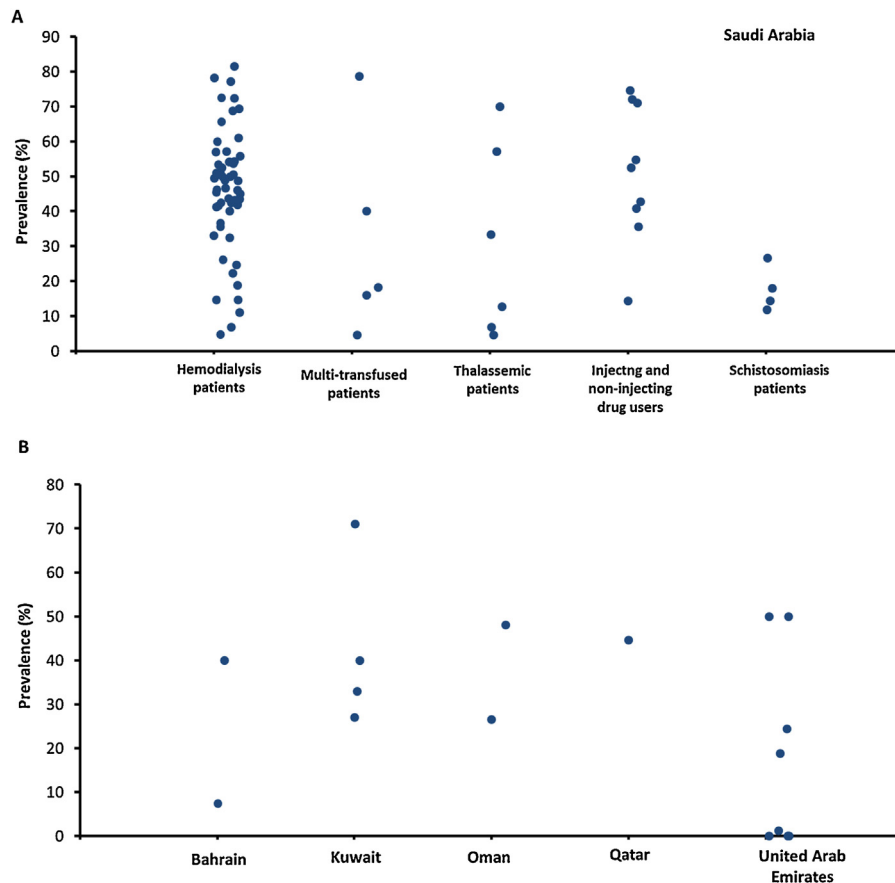


Figure 2. Distribution of hepatitis C virus (HCV) prevalence among high-risk groups in the Arabian Gulf countries. (A) HCV prevalence in the different high-risk groups in Saudi Arabia. (B) HCV prevalence in the high-risk groups of the remaining five Arabian Gulf countries: Bahrain, Kuwait, Oman, Qatar, and the United Arab Emirates. Few studies stratified by sub-groups were identified for countries other than Saudi Arabia; they were, therefore, grouped together in panel B.

measured HCV prevalence in a mixture of Bahraini and Saudi blood donors and reported a low prevalence of 0.3%.^{23,24}

3.2.2. Saudi Arabia

Saudi Arabia is the largest country in the region by population and area. Of the 442 HCV prevalence measures from this country reported in 120 records, 81 were among high-risk populations, 32 among intermediate-risk populations, 60 among special clinical populations, and 269 among general populations.

Figure 2A depicts the range of HCV prevalence among the different high-risk population subgroups in Saudi Arabia. HCV prevalence in hemodialysis patients ranged from 4.8% to as high as 84.6%. Among multi-transfused patients, HCV prevalence ranged between 4.6% and 78.6%. The lowest HCV prevalence (4.6%) was reported in a recent study by Zaher and Adam, which was conducted among multi-transfused children with a mean age of 12.9 years.²⁵ A majority of the studies conducted among thalassemics in Saudi Arabia also involved children and young adults. HCV prevalence among thalassemics was between 4.6% and 70%.

Five studies conducted among PWID in Saudi Arabia were identified. HCV prevalence ranged between 14.4% and 74.6%. The most recent study, estimating the prevalence in a combined population of injecting and non-injecting drug users, reported a prevalence of 35.6% and RNA prevalence of 29.9%.²⁶

Supplementary Material SM 7 depicts the range of HCV prevalence among intermediate-risk and special clinical populations in Saudi Arabia. Among populations at intermediate risk, Arif et al. reported a prevalence of 0% in household contacts of HCV

patients without CLD compared to 1.6% among household contacts of HCV patients with CLD.²⁷ Hospital attendees had a prevalence between 0.2% and 22.5%. The prevalence varied with age and nationality, with the highest prevalence observed among the 45–54-year-olds (15%) and among Egyptians (22.5%). HCV prevalence among HCWs ranged from 0% to 3.2%. Two studies reported HCV prevalence in populations with sexually transmitted diseases, reporting a high prevalence of 12%²⁸ and 15.9%.²⁹

High HCV prevalence was observed among special clinical populations. HCV prevalence among acute viral hepatitis patients ranged from 0% to 74.4%. Prevalence among HCC patients was between 4.4% and 62%, among non-Hodgkin's lymphoma patients was between 0% and 21%, and among lichen planus patients was between 9.8% and 26.3%. A study conducted in children 1–12 years of age undergoing chemotherapy reported a high prevalence of 11.3%.³⁰ Only one study investigated HCV prevalence among schistosomiasis patients.³¹ HCV prevalence in the overall study population was 18.0%: 11.8% among Saudi patients, 26.7% among Egyptian patients, and 14.3% among patients of other Middle Eastern nationalities.³¹

There is large variability in HCV prevalence among the different general population groups in Saudi Arabia. The prevalence ranged from 0% to 34.0% (Figure 3). Among blood donors, HCV prevalence was between 0% and 34.0%. Prevalence among pregnant women in two studies was 0.1%³² and 4.6%,²⁹ and among college students was between 0.03% and 0.4%. Higher HCV prevalence was observed among expatriates living in Saudi Arabia than among Saudi nationals (Figure 3, **Supplementary Material 8A**). **Supplementary Material SM 8B** depicts the range

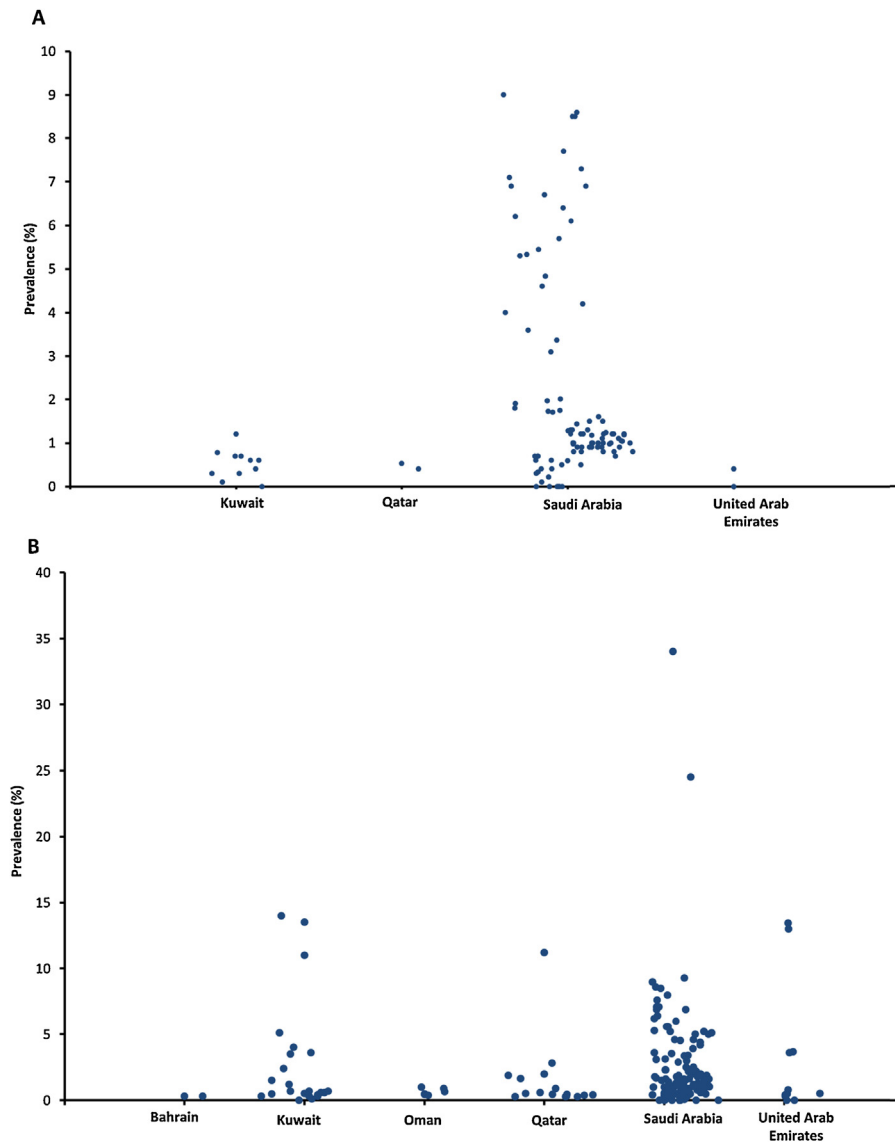


Figure 3. Distribution of hepatitis C virus (HCV) prevalence among general population groups in the Arabian Gulf countries. (A) Among country nationals only for countries from which this information was available. (B) Among the entire resident populations of nationals and expatriates.

of prevalence by nationality in studies for which this information was available. Egyptians had by far the highest HCV prevalence, reported at 8.0% to 34.0%, followed by Saudis at 0.2% to 7.3% and Indians at 0% to 7.1%.

3.2.3. Kuwait

Nine reports estimated HCV prevalence in different population groups in Kuwait, four of which reported the prevalence among high-risk populations. Figure 2B depicts the range of HCV prevalence in high-risk populations in Kuwait. A high prevalence was observed among hemodialysis patients, ranging between 27% and 71% (Figure 2B). Only one study was conducted among thalassemic patients, reporting a prevalence of 33%.³³

With regard to the populations at intermediate risk, Chehadeh et al. noted a prevalence of 7% among diabetics.³⁴ Only one study was conducted among HCWs, reporting a prevalence of 0.9%.³⁵ High HCV prevalence was observed among special clinical populations, ranging from 5.6% to 60.6%. **Supplementary Material SM 7** depicts the range of HCV prevalence among intermediate-risk and special clinical populations in Kuwait.

With regard to the general population groups, HCV prevalence among blood donors ranged from 0.1% to 14.0% (Figure 3). Overall,

a lower prevalence was observed among Kuwaiti nationals compared to expatriates residing in the country (Figure 3, **Supplementary Material SM 8A**). In a recent study conducted among 8561 Kuwaiti and 4237 non-Kuwaiti Arab first-time blood donors, HCV prevalence was 0.8% among Kuwaitis and 5.4% among non-Kuwaiti Arabs.³⁶

3.2.4. Oman

Seven articles reported HCV prevalence in Oman, two of which reported on high-risk populations (Figure 2B). The first study was among hemodialysis patients and reported a prevalence of 26.5%.³⁷ The second was among PWID and reported a prevalence of 48.05%, but the prevalence was based on self-report.³⁸

No HCV was detected in a study conducted among medical students.³⁹ A recent study conducted in a special clinical population group (immune thrombocytopenia patients) reported a prevalence of 3.1%.⁴⁰ **Supplementary Material SM 7** depicts the range of HCV prevalence among intermediate-risk and special clinical populations in Oman.

Overall, HCV prevalence among the general population groups in Oman, nationals and expatriates, was below 1%, ranging between 0.4% and 0.9% in blood donors (Figure 3B).

3.2.5. Qatar

Of eight reported studies estimating HCV prevalence in Qatar, only one was conducted in a high-risk population (Figure 2B). The study reported a high HCV prevalence of 44.6% among hemodialysis patients.⁴¹

High HCV prevalence was also reported among special clinical population groups, with a range of 9% to 30.6%. A recent study by Al Mannai and Riad reported a prevalence of 9% among lichen planus patients.⁴² Khan et al. reported a prevalence of 25.8% among cirrhosis patients.⁴³ **Supplementary Material** SM 7B depicts the range of HCV prevalence among special clinical populations in Qatar.

Four reports indicated HCV prevalence in general population groups in Qatar. Two studies were conducted among blood donors of different nationalities. Overall, HCV prevalence among general population groups, nationals and expatriates, ranged from 0.3% to 11.2% (Figure 3). **Supplementary Material** SM 8A compares HCV prevalence between Qatari nationals and expatriate residents for a number of studies for which this information was available. Variation in HCV prevalence between Qatari nationals and expatriate residents was reported in two studies.^{44,45} The overall HCV prevalence among 3352 blood donors was 2.8%, however the prevalence was only 0.4% among the Qatari blood donor subgroup.⁴⁴ Similarly, Fawzi et al. reported a 0.5% HCV prevalence among Qatari and 1.9% among non-Qatari blood donors, with the highest prevalence being reported among Egyptian blood donors (11.2%).⁴⁵

3.2.6. United Arab Emirates

Twelve reports measuring HCV prevalence in UAE were identified, of which three reported the HCV prevalence among high-risk population groups. Figure 2B depicts the range of HCV prevalence in high-risk populations in UAE. One study was conducted among hemodialysis patients and reported a prevalence of 24.4%.⁴⁶ A high HCV prevalence of 18.8% was reported among thalassemic children.⁴⁷

High HCV prevalence was also reported among intermediate-risk groups and special clinical populations in UAE. A prevalence of 7.7% was reported in children of HCV-positive Egyptian women residing in UAE, 73.9% in their spouses, and 26.8% in their other household contacts.⁴⁸ A recent study conducted by Abro et al. reported a low HCV prevalence of 1.2% among acute viral hepatitis patients.⁴⁹ The prevalence was 0% among UAE nationals, but as high as 50% among Pakistani nationals.⁴⁹ The prevalence among CLD patients was 43.7%.⁵⁰ **Supplementary Material** SM 7 depicts the range of HCV prevalence among intermediate-risk and special clinical populations in UAE.

Figure 3 displays the distribution of HCV prevalence in the general population groups in UAE for both nationals alone and mixed populations of nationals and expatriates. Overall, HCV prevalence in the general population groups ranged between 0% and 13.5% (Figure 3). It was higher among expatriates compared to nationals (Figure 3; **Supplementary Material** SM 8A). Newson-Smith reported a prevalence of 4.5% among Egyptians and 0.8% among other offshore gas and oil workers.⁵¹

3.3. HCV incidence overview

Only one study reported HCV incidence in the Arabian Gulf region. The study, conducted in 1995, examined HCV incidence in a dialysis unit in UAE and estimated it at 0.95 per 100 person-months.⁴⁶

3.4. Risk factors

Risk factors were most typically identified in studies conducted among high-risk populations. These included dialysis patients and

multi-transfused patients. The main risk factors consistently cited for HCV exposure were age,^{37,41,52–63} duration on dialysis,^{37,41,52–63} and the number of blood transfusions.^{22,53,54,56,60,61,64,65}

3.5. HCV genotypes

Genotype 4 is the most common HCV genotype reported in Saudi Arabia, Kuwait, and Qatar.^{66–69} According to a study by Messina et al., HCV genotype 4 accounts for 48% of HCV infections in Saudi Arabia, 56% of infections in Kuwait, and all infections in Qatar (100%).⁶⁷ In both Saudi Arabia and Kuwait, genotype 1 is the second most frequent genotype.⁶⁷ In Bahrain and UAE, however, genotype 1 is the most common genotype, accounting for 67% of HCV infections in Bahrain^{23,67} and almost 50% of infections in UAE.^{67,70} Genotype 2 is the second most common genotype in Bahrain,⁶⁷ while genotype 3 is the second most common genotype in UAE.^{67,70} No data on genotypes were available for Oman.⁶⁷

3.6. National and regional population-level HCV prevalence estimates

Pooled HCV population-level prevalence estimates stratified by country and nationality (nationals versus nationals and expatriates) are presented in Table 1 and Figure 4A, B. For Gulf country nationals alone in all countries for which information on nationality was available, the pooled HCV prevalence estimate for the whole region was 1.35% (95% CI 1.15–1.56). The pooled country-specific prevalence estimate among nationals was 0.24% (95% CI 0.02–0.63) for UAE, 0.44% (95% CI 0.29–0.62) for Kuwait, 0.51% (95% CI 0.43–0.59) for Qatar, and 1.65% (95% CI 1.40–1.91) for Saudi Arabia. No data on nationality were available for Bahrain or Oman, so no pooled estimates for nationals only could be calculated. **Supplementary Material** SM 9–11 show forest plots depicting the study-specific estimates as well as the meta-analysis estimates for nationals only.

With the inclusion of all general population prevalence measures regardless of nationality, the pooled HCV prevalence estimate for the whole region, among the resident population of nationals and expatriates, was 1.50% (95% CI 1.30–1.70). The country-specific pooled HCV prevalence estimate, among the resident population of nationals and expatriates, was 0.30% (95% CI 0.23–0.38) for Bahrain, 0.41% (95% CI 0.35–0.46) for Oman, 1.06% (95% CI 0.51–1.81) for Qatar, 1.45% (95% CI 0.75–2.34) for Kuwait, 1.63% (95% CI 1.42–1.84) for Saudi Arabia, and 1.64% (95% CI 0.96–2.49) for UAE. **Supplementary Material** SM 12–15 show forest plots depicting the study-specific estimates as well as the meta-analysis estimates for the entire resident populations.

Variations in HCV prevalence were observed in Saudi Arabia. Figure 4C displays the pooled HCV prevalence estimates and 95% CI for the five geographic regions of Saudi Arabia. A higher mean HCV prevalence was observed among the populations residing in the southwestern and southern parts of Saudi Arabia compared to the other regions.

4. Discussion

This is the first systematic review and data synthesis of HCV epidemiology in the Arabian Gulf region. The national population-level HCV prevalence in each of the Arabian Gulf countries was also estimated. With the recent remarkable successes in HCV treatment,^{71–74} these findings take on additional importance by providing the evidence base necessary for health services planning and the outlining of HCV policy guidelines, as well as the design and implementation of HCV treatment and prevention programs.

The results presented here show that the overall HCV prevalence in this region is at a level of about 1%, which is comparable to prevalence levels observed globally, including those

Table 1
Pooled hepatitis C virus prevalence in general population groups for each of the Arabian Gulf countries, among nationals only and among the entire resident populations of both nationals and expatriates

Category	No. of data points	No. of reports	No. tested for HCV antibody	No. HCV antibody-positive	HCV prevalence, % (95% CI)	I ² , % (95% CI)	p-Value ^a
Country nationals only							
All countries	70	33	852 836	9223	1.35 (1.15–1.56)	98.1 (97.9–98.3)	<0.001
Bahrain ^b	-	-	-	-	-	-	-
Saudi Arabia	57	27	808 787	8994	1.65 (1.40–1.91)	98.4 (98.2–98.5)	<0.001
Kuwait	9	2	12 853	67	0.44 (0.29–0.62)	39.9 (0.0–72.3)	0.10
Oman ^b	-	-	-	-	-	-	-
Qatar	2	2	29 764	157	0.51 (0.43–0.59)	0.0 (0.0–0.0)	0.81
United Arab Emirates	2	2	1432	5	0.24 (0.02–0.63)	0.0 (0.0–0.0)	0.50
Resident population (nationals and expatriates)							
All countries	183	78	1 574 036	16 347	1.50 (1.30–1.70)	98.7 (98.6–98.8)	<0.001
Bahrain ^c	2	2	21 125	63	0.30 (0.23–0.38)	0.0 (0.0–0.0)	0.96
Saudi Arabia	126	51	999 127	11 582	1.63 (1.42–1.84)	97.8 (97.6–97.9)	<0.001
Kuwait	22	5	44 772	939	1.45 (0.75–2.34)	97.6 (97.1–98.1)	<0.001
Oman	6	6	64 530	84	0.41 (0.35–0.46)	23.4 (0.0–67.4)	0.26
Qatar	16	4	153 704	2482	1.06 (0.51–1.81)	99.3 (99.2–99.4)	<0.001
United Arab Emirates	11	10	290 778	865	1.64 (0.96–2.49)	99.4 (99.3–99.5)	<0.001

HCV, hepatitis C virus; CI, confidence interval.

^a p-Value <0.10 considered statistically significant, indicating that the variation between pooled measures is due to heterogeneity rather than chance.

^b No studies provided numbers on HCV prevalence among nationals only.

^c All studies for Bahrain included a study population that was a mix of Bahrainis and Saudis.

of developed and developing countries.^{2,75} The regional HCV prevalence was estimated at 1.4% among nationals and at 1.5% among the resident population of nationals and expatriates. The country-specific HCV prevalence among nationals ranged from as low as 0.2% in UAE to as high as 1.7% in Saudi Arabia. By also including the expatriate populations, the country-specific HCV prevalence ranged from as low as 0.3% in Bahrain to as high as 1.6% in UAE.

The higher HCV prevalence estimates among some of the expatriate populations in some of the countries appear to reflect the higher HCV prevalence in the countries of origin of these expatriates. For example, the high HCV prevalence of 34.0%⁷⁶ among Egyptian blood donors in Saudi Arabia and 11.2%⁴⁵ among Egyptian blood donors in Qatar appears to reflect the high HCV prevalence in Egypt. At 14.7%, Egypt has the highest HCV prevalence worldwide.^{1,3} Exposure to the infection has probably occurred in the countries of origin and not in the host countries. This pattern has also been observed by Perumalswami et al.: in a recent study conducted in New York City, they observed an HCV prevalence of 15.6% among Egyptian-born persons living in New York and a strong association between HCV exposure and the number of years resident in Egypt.⁷⁷ Although all Gulf countries have mandated HCV screening prior to obtaining residency permits, migrants who test positive for HCV antibody are not necessarily deported. Moreover, those who became residents before the introduction of mandatory screening in the mid 1990s are usually allowed continuous residency even if found to be HCV antibody-positive.

The distribution of HCV genotypes in this region appears also to reflect in part the HCV genotype distributions in the expatriates' countries of origin. Genotype 4 appears to be the most common HCV genotype in most countries in this region, followed by genotypes 1 and 3. HCV genotype 4 is by far the most common genotype in Egypt and is common in other MENA countries such as Iraq, Jordan, Lebanon, and Syria.^{10,66,67} Meanwhile, genotypes 1 and 3 are the most common genotypes in India, Nepal, and Pakistan,^{66,67} and there are large expatriate populations from these countries in the Arabian Gulf region. HCV genotype diversity therefore appears also to suggest exposure in the countries of origin.

The high HCV prevalence levels among some of the clinical populations are indicative of exposure in the medical setting.

Prevalence measures among hemodialysis patients ranged from 7.4%²³ to as high as 84.6%.⁷⁸ In the only incidence study identified in the region, HCV incidence in a dialysis unit in UAE was high at 0.95 per 100 person-months.⁴⁶ The main risk factors consistently cited for exposure to the infection across studies were duration on dialysis^{37,41,52–63} and history of blood transfusions.^{56,60,61,64,65}

It is difficult to ascertain the timing of exposure to HCV. It is conceivable that a large proportion of exposures may have occurred prior to the enforcement of stringent infection control and blood screening protocols, which were implemented starting in the 1990s. Regrettably, no nationally representative population-based studies with age-stratified prevalence estimates could be identified. Such studies may help identify changes in exposure to the infection across different age cohorts at different times, such as those identified in other countries.^{79–81} Regardless, there seems to be an indication of ongoing HCV transmission in the clinical setting that appears to be linked to less than optimal infection control practices, as highlighted by the high HCV prevalence reported in recent studies among children with a history of clinical procedures.^{25,47}

Injecting drug use is the major driver of HCV incidence and prevalence in developed countries.^{82,83} The estimated population proportion of PWID in the Arabian Gulf ranges between 0.16% in Bahrain and 0.30% in each of Kuwait, Oman, and UAE.⁸⁴ The population proportion of PWID in the whole MENA region is estimated at 0.24% – in the intermediate range compared to global levels.⁸⁴ There are few studies on HCV prevalence among PWID in the Arabian Gulf region, some of which have included other drug users; a study from Saudi Arabia reported HCV prevalence ranging between 40.8% and 74.6%⁸⁵ (**Supplementary Material** table SM 3). Given the population proportion of PWID and the epidemiological context of HCV infection as highlighted in this study, it does not seem that injecting drug use explains more than a minority of HCV exposures in this region.

Regional differences in HCV prevalence were identified in Saudi Arabia (**Figure 4C**). The southwestern and southern regions of the country are the two with the highest pooled HCV prevalence, especially Gizan Province.^{21,86} Al-Faleh et al. conducted a population-based survey of children (1 to 10 years of age) across Saudi Arabia and reported a high HCV prevalence of 5.7% in the city of Gizan, which was several fold higher than that of the rest of the

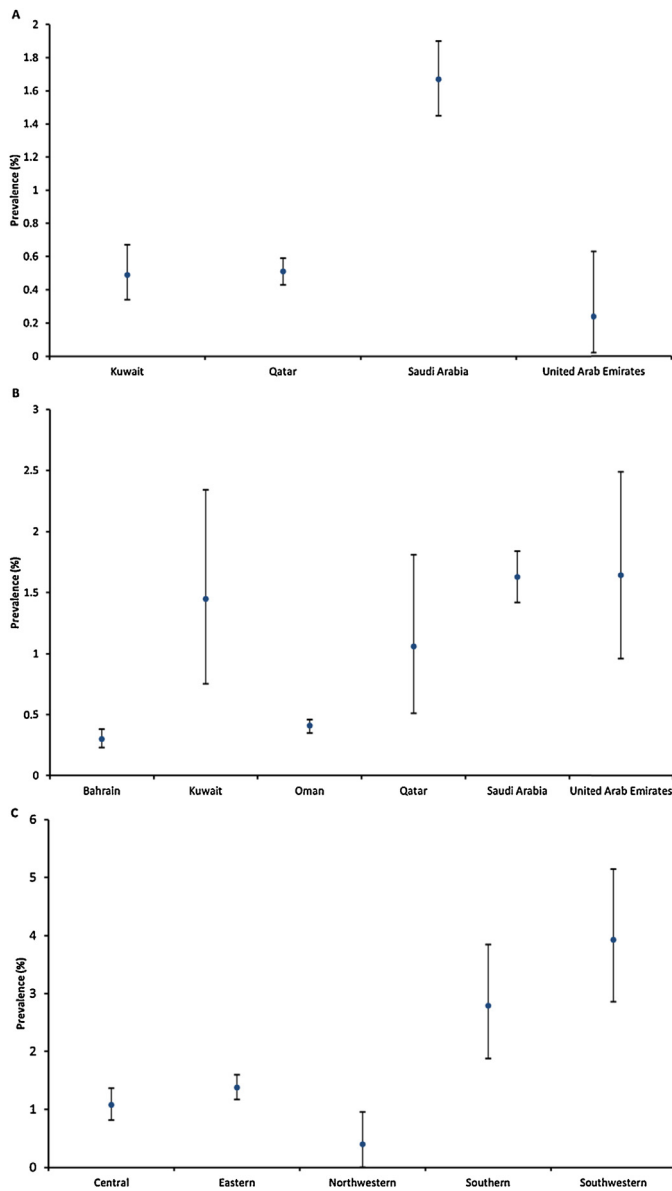


Figure 4. Pooled hepatitis C virus (HCV) prevalence and 95% confidence intervals for the general population groups of each of the six Arabian Gulf countries. (A) Among country nationals only for countries from which this information was available. (B) Among the entire resident populations of nationals and expatriates. (C) Among the different regions in Saudi Arabia.

country.²¹ A more recent study by Ayoola and Gadour also reported a rather high prevalence of 3.4% among healthy adult controls in Gizan.⁸⁶ Gizan appears also to be hyperendemic for hepatitis B virus,²¹ which shares overlapping epidemiology with HCV. While the specific modes of HCV exposure are not clear, and most likely they are medical-related exposures, the area of Gizan has been linked to folk blood-letting practices ('Hijama') that can increase the risk of blood-borne infections such as HCV.⁸⁷ The regional variations in prevalence in Saudi Arabia warrant further investigation and determination of the specific modes of HCV exposure.

Among the limitations of this study are the variability in the number of studies across countries and the low number of studies from Bahrain and Oman. The general population studies included in the meta-analyses may not have been representative of the whole population. Nearly all studies included convenience samples, and many of the studies were on blood donors. Convenience sampling often leads to a biased estimate of infection

prevalence. For example, HCV prevalence in blood donors may underestimate HCV prevalence in the whole population. It is conceivable that there could be a selection bias towards lower risk among blood donors, normally a healthy population. Future studies should use probability-based sampling methods, such as nationally representative population-based surveys, which would help yield accurate estimates of HCV prevalence in this region and identify the main risk factors of HCV exposure in the population. These surveys would help to draw a clearer and more complete picture of HCV epidemiology in this part of the world.

Genotype information was available from only a few studies, and therefore the genotype distribution described may have been biased by non-representative samples. The populations were classified into high-risk, intermediate-risk, and general population groups by convention.⁸ However, there is no established existing classification of risk for some populations, and the information available in some studies was not sufficient to determine the level of risk. In these situations, the level of risk was determined based on the authors' best judgment of the risk of exposure to HCV infection in this population. For example, clinical populations for which the risk of exposure was uncertain were classified into the independent category of 'special clinical populations'.

The meta-analyses highlighted substantial heterogeneity among the studies conducted in the general population groups. This is not surprising considering the differences between studies in terms of the populations studied, sampling methodology and recruitment, sample age distribution, year of study, location, and assay used.⁸ However, due to the relatively small number of outcome measures for each country, it was not possible to conduct a meaningful meta-regression analysis to identify the potential sources of variation explaining the observed heterogeneity.

In conclusion, despite variability in HCV prevalence across the Arabian Gulf countries, prevalence levels are similar to global levels. HCV prevalence among nationals appears to be around 1% and is generally lower than that among resident expatriate populations. The high HCV prevalence found in specific expatriate populations appears to reflect the higher prevalence in their countries of origin. Ongoing transmission appears to be concentrated in high-risk groups and is often linked to medical care. Injecting drug use is possibly a major contributor to HCV incidence in this region, but is not likely to explain more than a minority of prevalent infections.

These findings provide the evidence base necessary to inform health services planning, the articulation of HCV policy guidelines, and implementation of HCV programs to reduce transmission and decrease the burden of disease. Further research is needed to draw a more complete understanding of HCV epidemiology, such as through nationally representative population-based surveys. These surveys may identify modes of exposure, delineate spatial variability in prevalence, and assess HCV knowledge and attitudes, as has been done recently in Egypt.^{3,79,88–91} This is particularly relevant for Saudi Arabia, a large country where there appears to be spatial variability in HCV exposure. Since HCV prevalence in the Arabian Gulf countries is not high and is linked to specific settings, HCV prevention efforts should be targeted at infection control in the clinical setting and harm reduction among PWID.

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Author contributions: YM and SR conducted the literature review and data retrieval. YM conducted the extraction of data and data analysis, and wrote the first draft of the paper. LJA conceived and led the design of the study, analyses, and drafting of the article. All authors contributed to discussion of the results and writing of the manuscript.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.ijid.2016.03.012>.

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