

RESEARCH ARTICLE

Hepatitis C Virus Epidemiology in Djibouti, Somalia, Sudan, and Yemen: Systematic Review and Meta-Analysis

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Abstract

Objectives

To characterize hepatitis C virus (HCV) epidemiology and assess country-specific population-level HCV prevalence in four countries in the Middle East and North Africa (MENA) region: Djibouti, Somalia, Sudan, and Yemen.

Methods

Reports of HCV prevalence were systematically reviewed as per PRISMA guidelines. Pooled HCV prevalence estimates in different risk populations were conducted when the number of measures per risk category was at least five.

Results

We identified 101 prevalence estimates. Pooled HCV antibody prevalence in the general population in Somalia, Sudan and Yemen was 0.9% (95% confidence interval [95%CI]: 0.3%–1.9%), 1.0% (95%CI: 0.3%–1.9%) and 1.9% (95%CI: 1.4%–2.6%), respectively. The only general population study from Djibouti reported a prevalence of 0.3% (CI: 0.2%–0.4%) in blood donors. In high-risk populations (e.g., haemodialysis and haemophilia patients), pooled HCV prevalence was 17.3% (95%CI: 8.6%–28.2%) in Sudan. In Yemen, three studies of haemodialysis patients reported HCV prevalence between 40.0%–62.7%. In intermediate-risk populations (e.g., healthcare workers, in patients and men who have sex with men), pooled HCV prevalence was 1.7% (95%CI: 0.0%–4.9%) in Somalia and 0.6% (95% CI: 0.4%–0.8%) in Sudan.

Conclusion

National HCV prevalence in Yemen appears to be higher than in Djibouti, Somalia, and Sudan as well as most other MENA countries; but otherwise prevalence levels in this subregion are comparable to global levels. The high HCV prevalence in patients who have

had no role in the design, conduct, or analysis of the study.

Competing Interests: The authors have declared that no competing interests exist.

Abbreviations: 95%CI, 95% confidence interval; CLD, chronic liver disease; EMRO, WHO Regional Office for the Eastern Mediterranean; FSW, female sex workers; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; HCWs, healthcare workers; HD, haemodialysis; IAS, International AIDS Society; IBBS, integrated bio-behavioural HIV surveillance surveys; KSA, Kingdom of Saudi Arabia; MENA, Middle East and North Africa; MSM, men who have sex with men; n, number of studies; NHL, non-Hodgkin lymphoma; OR, odds ratio; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; p-value, probability value; PWID, people who inject drugs; ROB, risk of bias; SI, supporting information; SOS institution, Société Organisation Sociale institution; STD, sexually transmitted disease; UNAIDS, the Joint United Nations Programme on HIV/AIDS; WHO, World Health Organization.

undergone clinical care appears to reflect ongoing transmission in clinical settings. HCV prevalence in people who inject drugs remains unknown.

Introduction

The global distribution of hepatitis C virus (HCV) infection is the consequence of national and local circumstances that have facilitated or limited HCV transmission in different populations [1–3]. The geographical distribution of this infection appears to vary from one region to another. The Middle East and North Africa (MENA) region appears to have the highest HCV prevalence worldwide [4, 5] with Egypt recording the highest national prevalence in the adult population at 14.7% [6, 7]. While the epidemiology of this infection is well studied in Egypt [6, 7], the infection status in most other MENA countries is yet to be well understood.

By applying a methodology developed recently [8, 9], this study aims to characterize the epidemiology of HCV infection and to estimate the national population-level HCV antibody prevalence in Djibouti, Somalia, Sudan, and Yemen, a group of MENA countries that we have labelled conventionally as the Horn of Africa subregion of MENA. This group of MENA countries were studied within the framework of one study because of their geographic proximity. This study is part of a larger ongoing project—the MENA HCV Epidemiology Synthesis Project [7–14]—that aims to characterize the epidemiology of HCV across the MENA region and to inform public health policy and programming at the national and regional levels.

Materials and Methods

The protocol for this systematic review has been described elsewhere [8] and is registered at the International Prospective Register of Systematic Reviews under registration number CRD42014010318 [9]. The study methodology of the present article was also applied and refined in several previous studies of HCV epidemiology in different subregions and countries within MENA [7, 12–14]. We summarize our methodology in the following subsections. Further details can be found in the earlier descriptions and applications of this methodology [7–9, 12–14].

Data sources and search strategy

This review was conducted based on the items outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [15] (S1 Table). The search criteria are provided in S2 Table. As in previous studies [7, 12–14], we searched for English and non-English reports in PubMed, Embase and the World Health Organization (WHO) regional databases (WHO African Index Medicus [16] and WHO Index Medicus for the Eastern Mediterranean Region [17]) for entries up to May 17th, 2015. To identify further relevant reports, we screened all articles archived in online national scientific journals not indexed in PubMed or Embase (up to May 17th, 2015). These journals included the Yemeni Journal of Medical Sciences [18], the Sudan Journal of Medical Sciences [19] and the Sudan Medical Journal [20]. Moreover, the literature database of the MENA HIV/AIDS Epidemiology Synthesis Project was searched for potentially relevant country-level and international organizations' reports (up to April 14, 2015) [21, 22].

The database search was supplemented by checking references of the included reports and identified reviews. Lastly, we also searched the conference archives of the International AIDS Society conferences [23] and the 'Endemic and Emerging Viral Diseases of Priority in the Middle East and North Africa (MENA)' workshop [24] (up to May 17th, 2015).

Inclusion and exclusion criteria

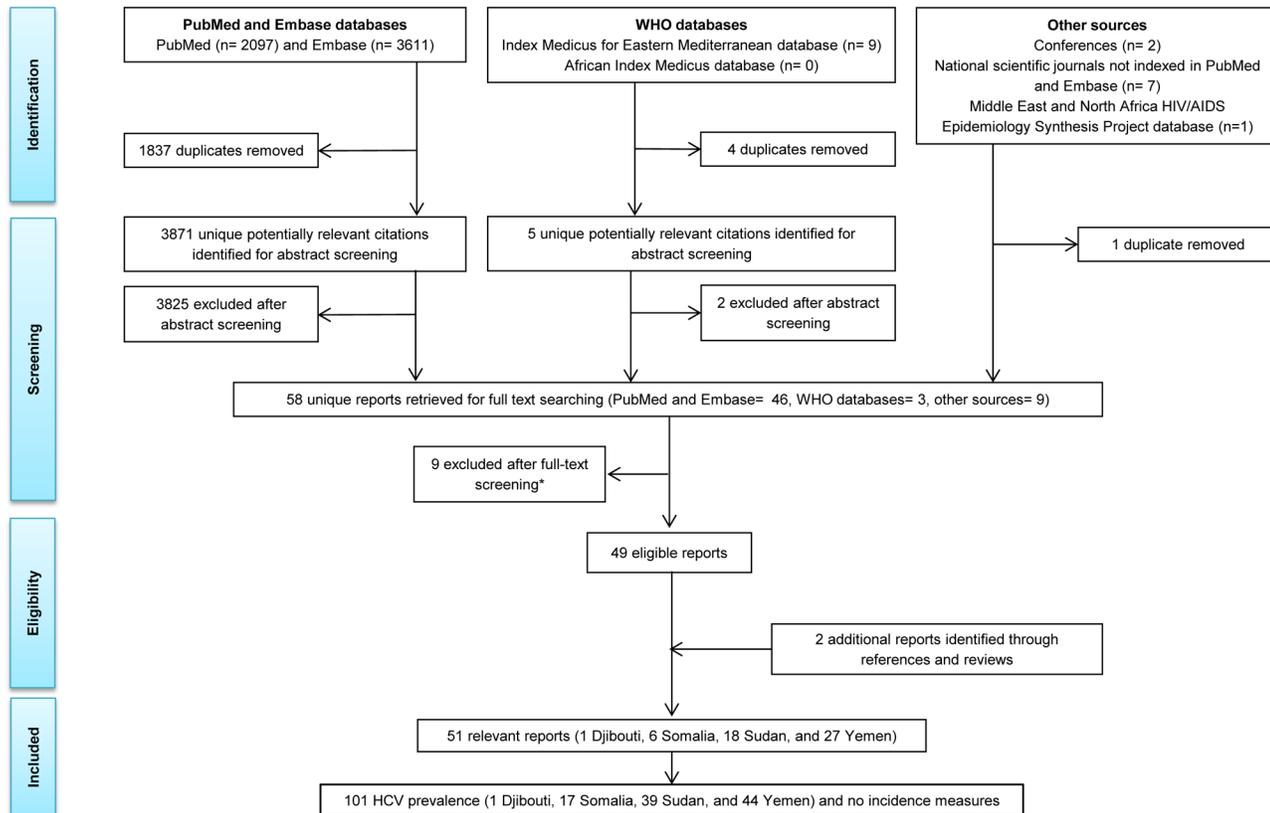
The inclusion and exclusion criteria were developed along the lines of our previous systematic reviews [7, 12–14]. Studies with primary data were eligible for inclusion if they included populations who are permanently residing in any of the countries of Djibouti, Somalia, Sudan and Yemen. Our systematic review did not include migrants from these countries who are residing elsewhere. Studies such as Shire *et al.* 2012 [25] among migrant Somalis in the United States did not fit our inclusion criteria. Our definition for the MENA region was based on the MENA definition of the Eastern Mediterranean Regional Office of the World Health Organization (EMRO/WHO), the Joint United Nations Programme on HIV/AIDS (UNAIDS), and the World Bank. Djibouti, Somalia, Sudan, and Yemen were grouped together as part of one study because of their geographic proximity and because they could not fit within the scope of the other sub-regional studies of the MENA HCV Epidemiology Synthesis Project [7, 10–14]. Although these countries were grouped in one article, we conducted the epidemiological analyses for each country separately. Sudan and South Sudan were considered as one country because the time period covered in this review extends well beyond the independence of South Sudan in 2011.

Other criteria for inclusion were availability of data on serological testing for HCV antibody and an estimate of HCV incidence or prevalence. Reports were considered ineligible if they were based on self-report, saliva testing, or classification of HCV as non-A non-B hepatitis. Case reports, case series, reviews, qualitative studies, editorials, commentaries, letters to editors, author replies and animal studies were excluded. Reports were included in the systematic review if the study sample size was greater than 15. In the meta-analyses however, we included from the systematic review studies only the studies that had a sample size greater than 25 for consistency with the other sub-regional analyses [10–14].

Study selection

References obtained through the search strategy were imported into a reference manager, Endnote [26], where duplicate reports were identified and excluded. The titles and abstracts of identified unique reports were screened for relevance by Karima Chaabna (KC). After title and abstract screening, full texts of the reports deemed relevant or potentially relevant were retrieved and assessed for eligibility for inclusion by KC. During this step, any remaining non-eligible reports were excluded and the reasons for their exclusion recorded (Fig 1).

Data extraction and synthesis. Relevant data were extracted by KC and checked for correctness by Silva Kouyoumjian (SK). Discrepancies were discussed and resolved by the study team. As in previous studies [7, 12–14], extracted data included reference details (author(s), year of publication, title, and journal), study location, year(s) of data collection, study design, sampling technique, population profile (such as blood donors and healthcare workers (HCWs)), socio-demographic characteristics of the population (sex and age), number of participants who were included and who did participate, response rate, name of the serological test used to determine HCV exposure, and raw results obtained for the primary outcome (HCV incidence or prevalence estimates). The following parameters were also recorded from included studies when available: HCV RNA incidence and prevalence estimates; HCV genotype frequency; and adjusted or unadjusted statistically significant (probability (p) value ≤ 0.05) risk factors for HCV exposure. Relevant data were extracted from abstracts for studies for which full texts could not be obtained even after contacting the authors. Decimal places of prevalence figures were reported in this article as reported in the original reports. Prevalence figures with more than one decimal place were rounded to one decimal place, with the exception of those below 0.1%. All meta-analyses used original raw numbers of cases and samples, with no rounding.



* Reasons for exclusion:

- Eligibility criteria not met (n = 6)
- Full-text could not be retrieved and abstract does not have data on relevant outcomes (n = 1)
- Abstract and full-text could not be retrieved (n = 1)
- Overlap with another already published study (n = 1)

Fig 1. Flow of report selection for HCV incidence and prevalence in Djibouti, Somalia, Sudan and Yemen, adapted from the PRISMA guidelines [15].

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In this systematic review, the word ‘report’ refers to a publication (article, country-level report, or conference abstract, among others) that presents one or several outcome measures, while the word ‘study’ refers to any one specific outcome measure. Several reports of the same outcome measure were identified as duplicates and counted as one study. HCV measures were treated and counted as separate studies if, within the same report, HCV measures were reported stratified by population subgroup, and/or sex, and/or study period, and/or region, and/or age.

As in the earlier studies [7, 12–14], extracted data were presented and analysed stratified by country and according to the study population’s risk of acquiring HCV infection as follows:

1. Populations at high risk: these include patients with a history of haemodialysis (HD), thalassaemia, haemophilia, multiple transfusions, or schistosomiasis. In addition, these high-risk populations included people who inject drugs (PWID).
2. Populations at intermediate risk: these include HCWs, patients with sexually transmitted diseases (STDs), hospitalized patients, female sex workers (FSWs), and men who have sex with men (MSM).

3. Populations at low-risk (general populations): these include pregnant women, antenatal clinic attendees, blood donors, tuberculosis outpatients, military personnel, controls in case-control studies, and healthy adults and children among other general populations.
4. Special clinical populations: these include patients with specific diseases that could be related to HCV infection such as chronic liver disease (CLD), viral hepatitis, cirrhosis, hepatocellular carcinoma (HCC), and non-Hodgkin lymphoma (NHL). This category also includes other clinical populations who could have been exposed to HCV in clinical settings, such as patients with leprosy or those treated in surgical departments, but at variable risk of exposure. In essence, this category encompasses patients with clinical conditions associated with HCV infection or patients at risk of exposure to HCV in clinical settings but with an uncertain level of exposure making it difficult to classify them under the former three risk population groups.
5. Mixed populations: these comprise samples of persons with variable HCV infection risk that is a mix of the other four population groups.

Quantitative analysis

Data analyses were conducted in R v.3.1.1. [27] using the *meta* package [28] and in Stata/SE 13.1 using the *metan* command [29]. The 95% confidence interval (95%CI) for HCV prevalence estimate in each individual included study was calculated using the Clopper-Pearson (binomial) method [30]. Studies presenting a minimum sample size of 25 participants were included in the meta-analysis. HCV prevalence estimates were pooled when at least five studies were included in each risk population category for each country. All meta-analyses were conducted using random-effects models, to account for expected heterogeneity in effect size across studies. HCV prevalence estimates were weighed by the inverse-variance of the double-arcsine transformed proportions [31], according to the method described by DerSimonian and Laird [32]. The back-transformed pooled mean proportions were calculated using Miller's inverse transformation with the harmonic mean of the sample sizes [33]. The value 0.5 was added to all cell frequencies of studies with a zero cell count [34]. Sensitivity analysis was conducted using the value of 0.01, instead of 0.5, but the same mean proportions and their 95%CIs were obtained. Forest plots for all meta-analyses were generated.

To assess heterogeneity across studies, forest plots were inspected visually and Cochran's Q test was conducted [35]. A two-sided Q test *p*-value of <0.10 was considered as significant. I^2 heterogeneity measure and its 95%CI were calculated to assess the magnitude of between-study variation that is due to heterogeneity in effect size rather than chance [36]. The prediction interval was calculated to describe the distribution of true effects around the mean [37–39]. In situations of high heterogeneity and potential non-random biases, such as possibly in HCV prevalence measures in a given risk population, the prediction interval may provide a more interpretable summary of the variation in effect size in existing studies and potential true population mean.

A meta-regression [40] was undertaken to identify study-level factors contributing to the between-study heterogeneity in the pooled mean general population prevalence estimate. The following factors were entered into univariable and multivariable models: country, subpopulation within the low risk population, study design, study site, and precision of the measure. These factors were selected based on being reported in at least ten studies. These factors were included in the multivariable model if the *p*-value was <0.10.

National population-level HCV prevalence was estimated using individual study estimates of HCV prevalence in the general population in each country. Sensitivity analyses were conducted

to assess the impact of excluding blood donor studies on pooled mean HCV prevalence estimates, and to assess the impact of excluding studies with a sample size lower than 1,000 and those published before 2000. The latter sensitivity analysis was motivated by the inclusion criteria in global estimations for HCV prevalence conducted recently by Gower *et al.* [41].

Quality assessment

Per earlier developed methodology [8, 9], the quality of individual HCV prevalence estimates was determined by assessing the risk of bias (ROB) for each study and by evaluating the precision of each reported measure. ROB assessment was conducted by assessing the sources of bias that may affect the pooled mean estimates. Based on the Cochrane approach [40], each HCV prevalence measure was classified as having a low, high, or unclear ROB in three domains: sampling methodology, HCV infection ascertainment, and response rate. Response rate was defined as the number of tested individuals divided by the number of all persons invited to participate in the study [42]. ROB was considered low if (1) sampling was probability-based, (2) HCV was ascertained by biological assays, and (3) response rate was $\geq 80\%$ or, for studies using respondent-driven sampling, $\geq 80\%$ of the target sample size was reached. Studies with missing information for a specific domain were classified as having unclear ROB for that specific domain.

A study HCV prevalence estimate was considered as having good precision if the number of HCV tested individuals was at least 100. For a median HCV prevalence in the general population in this MENA subregion of 1.3% (see [Results](#)), this implies a 95%CI of 0%-5%.

Results

Search results

The process of study selection was based on PRISMA guidelines [15] (Fig 1). We identified a total of 5,708 citations: 2,097 through PubMed, 3,611 through Embase, nine through WHO databases, two through conference databases, seven through national scientific journals not indexed in PubMed or Embase, and one through the MENA HIV/AIDS Epidemiology Synthesis Project database. A total of 58 records were identified as relevant or potentially relevant after removing duplicates and screening the titles and abstracts of remaining records. Out of these 58 records, 49 were eligible for inclusion in the systematic review at the full-text screening stage. The remaining were excluded for multiple reasons such as not meeting the eligibility criteria, absence of data on relevant indicators in the full text and/or abstract, failure to retrieve the full text and/or abstract of a record, and duplication of another study included in the review. Two additional records were identified through screening the bibliographies of studies and reviews [43, 44]. To sum up, a total of 51 eligible reports and 101 HCV prevalence studies were included in the systematic review. These included one study in Djibouti, 17 studies in Somalia, 39 studies in Sudan and 44 studies in Yemen. No HCV incidence study was identified in this subregion.

HCV prevalence overview

HCV prevalence ranged from 2.2% to 62.7% (number of studies (n) = 11 and median = 18.4%) in high-risk populations and from 6.3% to 40.3% (n = 17 and median = 17.8%) in special clinical populations. Meanwhile, HCV prevalence ranged from 0% to 5.8% (n = 31 and median = 0.5%) in intermediate-risk populations and from 0% to 8.5% (n = 42 and median = 1.3%) in general populations. In what follows we present an overview of country-level HCV prevalence studies.

Djibouti. The single study from Djibouti reported a prevalence of 0.3%. The majority of the sample were male blood donors (17–65 years old) [43] (Table 1).

Somalia. There were no studies in high risk populations. Among intermediate-risk populations, HCV prevalence was in the range of 0%–7% ($n = 5$ and median = 2.4%) [44–46] (Table 2). The highest HCV prevalence of 7% was recorded for hospitalized adults and the lowest of 0% was reported among hospitalized children [44]. In special clinical populations, HCV prevalence was high at 14.5% [44] and 40.3% [47] among patients with CLD (Table 2).

In the general population, rather low HCV prevalence was reported in most studies ($n = 9$ and median = 1%) [44–49] (Table 1). The lowest HCV prevalence of 0% was reported in a group of children from a government-operated residence for abandoned children [48]; while the highest prevalence of 6.4% was reported in controls in a case-control study [47] (Table 1). The most recent study, conducted in 2011, tested 12,759 blood donors and reported a prevalence of 0.5% [49].

Sudan. In high-risk populations, most studies reported high HCV prevalence in the range of 4.5%–34.9% ($n = 6$ and median = 18.4%) [50–56] (Table 2). High HCV prevalence was reported in clinical populations including HD patients (between 8.5% and 34.9%) [54–56] and haemophilia patients (13%) [53].

In intermediate-risk populations, most studies reported low HCV prevalence in the range of 0%–5.9% ($n = 23$ and median = 0.5%) [54, 56–60] (Table 2). The majority of HCV prevalence estimates were in MSM and FSWs [57]. The highest prevalence was reported in MSM and FSWs from South Darfur (5.9% and 5.1%, respectively) [57] and in HCWs in a dialysis centre in Khartoum (5.4%) [56].

In special clinical populations, one study reported an HCV prevalence of 11% in patients with HCC [61] and another study reported an HCV prevalence of 6.3% in pregnant women with acute viral hepatitis [62] (Table 2).

In the general population, rather low HCV prevalence was reported in most studies that ranged from 0%–4% ($n = 7$ and median = 1.3%) [50, 61, 63–67] (Table 1). The lowest prevalence was observed in a study among blood donors at 0% [66] and in a study among pregnant women at 0.6% [63], while the highest prevalence of 4% was reported in non-*Schistosoma*-infected controls [50].

Yemen. In high-risk populations, three studies measured HCV prevalence among HD patients and estimated it at a high level of 40% [68], 40.2% [69] and 62.7% [70] (Table 2). In intermediate-risk populations, three studies reported HCV prevalence among HCWs at 0.5% [68], 1.3% [71] and 3.5% [72] (Table 2). In special clinical populations, overall high HCV prevalence was observed in the range of 6.4%–38.2% ($n = 13$ and median = 17.9%) [68, 70, 73–82] (Table 2). The highest prevalence estimates were reported in patients with acute and chronic hepatitis at 37.1% [76] and in patients with HCC at 38.2% [79].

In the general population, HCV prevalence was in the range of 0%–8.5% ($n = 25$ and median = 1.3%) [70, 73, 76, 78, 80, 83–92] (Table 1). The highest prevalence at 8.5% was reported in 400 pregnant women in Sana'a in 2011 [85]. The study with the largest sample size (20,329 individuals) reported a prevalence of 4.3% among male controls recruited for a case-control study in 2005–2007.

Pooled mean HCV prevalence estimates

The pooled country-specific estimates for the national population-level HCV prevalence, based on pooling the general population measures, were: 0.9% (95%CI: 0.3%–1.9%) in Somalia, 1.0% (95%CI: 0.3%–1.9%) in Sudan and 1.9 (95%CI: 1.4%–2.6%) in Yemen. It was also 1.5% (95%CI: 1.0%–2.2%) in this MENA subregion as a whole (Table 3). The corresponding prediction

Table 1. Studies reporting HCV prevalence in the general population in Djibouti, Somalia, Sudan and Yemen.

Author, Year	Location	Study period	Study design	Population characteristic	Sample size	Prevalence (%)*
Djibouti						
Dray, 2005 (43)	Djibouti	1998–2000	Cross-sectional	Blood donors	8,057	0.3
Somalia						
Bile, 1992 (48)	Mogadishu	1987	Cross-sectional	Children in government-operated residence for abandoned children in SOS institution (boy and girls)	76	0
EMRO, 2011 (49)	National	-	Cross-sectional	Blood donors	12,759	0.5
Nur, 2000 (45)	Mogadishu	1995	Cross-sectional	Blood donors	157	0.6
Aceti, 1993 (44)	Mogadishu	1988–1990	Retrospective	Blood donors (nursing school students) no history of parenteral exposure to blood or blood products, nor clinical or pathological picture compatible with viral hepatitis, nor any other apparent indication of liver disease.	309	1
Bile, 1992 (48)	Mogadishu	1987	Cross-sectional	Children in government-operated residence for abandoned children in Shebeli (girls)	287	1
Watts, 1994 (46)	Mogadishu, Merca and Chismayu	1990	Cross-sectional	Military personnel	79	1.3
Bile, 1992 (48)	Mogadishu	1987	Cross-sectional	Children in government-operated residence for abandoned children in Shebeli (boys)	309	1.9
Watts, 1994 (46)	Mogadishu, Merca and Chismayu	1990	Cross-sectional	Outpatients with tuberculosis	43	2.3
Bile, 1993 (47)	Mogadishu	1989	Case-control	Control patients treated from different hospital departments	62	6.4
Sudan						
Elfaki, 2008 (66)	El Obeid	-	Cross-sectional	Blood donors (farmers, shepherds, soldiers, lorry drivers, labours, employees, and others)	260	0
Elsheikh, 2007 (63)	Omdurman	2006	Cross-sectional	Pregnant women	423	0.6
Abou, 2009 (64)	Nyala (Dar Fur)	2007	Cross-sectional	Blood donors	400	1
Osman, 2014 (67)	Gezira	2011	Cross-sectional	Women attending maternity hospital (patients with antepartum haemorrhage, hypertension and diabetes mellitus excluded)	396	1.3
Nagi, 2007 (65)	Shendi	2005	Cross-sectional	Blood donors (males)	78	1.3
Omer, 2001 (61)	Gezira and North Kordofan	1996–1998	Case-control	Control from general population	199	2
Mohamedani, 2014 (50)	Gezira	-	Case-control	Non- <i>Schistosoma</i> infected controls	100	4
Yemen						
Gray, 1999 (89)	Hajjah	1992	Cross-sectional	General population	253	0
Sallam, 2003 (84)	Sana'a	1999–2002	Cross-sectional	Blood donors (males)	493	0.2
Sallam, 2003 (84)	Aden	1999–2002	Cross-sectional	Blood donors (males)	494	0.6
Saghir, 2012 (92)	Hobeidah	2009–2010	Cross-sectional	Blood donors	564	0.7
Selm, 2010 (69)	Aden	2007	Case-control	Control consisting of blood donors (males)	100	0.8

(Continued)

Table 1. (Continued)

Author, Year	Location	Study period	Study design	Population characteristic	Sample size	Prevalence (%)*
Saghir, 2012 (92)	Hobeidah	2008–2009	Cross-sectional	Blood donors	919	0.9
Gray, 1999 (89)	Ibb	1992	Cross-sectional	General population from Al Homaadi village	175	1
Gray, 1999 (89)	Ibb	1992	Cross-sectional	General population from Mouthan village	158	1
Oshaish, 2008 (91)	Taiz	-	Cross-sectional	Blood donors	1,000	1
El Guneid, 1993 (80)	Taiz	-	Cross-sectional	Blood donors (males)	294	1
Al-Waleedi, 2012 (83)	Aden	2007–2008	Cross-sectional	Blood donors	469	1.3
Gacche, 2012 (94)	Ibb	2010–2011	Cross-sectional	Healthy subjects	2,379	1.3
Sallam, 2003 (84)	Sana'a	1999–2002	Cross-sectional	African migrant community living in a shantytown	593	1.3
Omer, 2010 (88)	Aden	2007	Cross-sectional	Blood donors	5,825	2
Haidar, 2002 (68)	Hajjah	1997–1999	Cross-sectional	Blood donors	2,434	2
Al-Shamiri, 2011 (87)	Taiz	2007–2009	Cross-sectional	Children at school	141	2.1
Alodini, 2012 (90)	Sana'a	2010	Cross-sectional	Blood donors	3,000	3
El Guneid, 1993 (80)	Taiz	-	Cross-sectional	Healthy pregnant women	243	3.3
Salem, 2009 (78)	Sana'a	2005–2007	Case-control	Control patients—females—treated from different hospital departments (patients coming from different parts of the country)	8,055	3.5
Denis, 1994 (73)	.	1988–1990	Case-control	Control patients (blood donors and pregnant women)	51	3.9
Al-Moslih, 2001 (76)	Sana'a	-	Case-control	Control patients (no history of liver disease)	120	4.2
Salem, 2009 (78)	Sana'a	2005–2007	Case-control	Control patients—males—treated from different hospital departments (patients coming from different parts of the country)	20,329	4.3
Sallam, 2003 (84)	Soqatra Island	1999–2002	Cross-sectional	Residents of Soqatra	99	5
Scott, 1992 (86)	Sana'a, Hajjah, Taiz and Hobeidah	1988	Cross-sectional	Healthy children and adults	348	6
Murad, 2013 (85)	Sana'a	2011	Cross-sectional	Pregnant women at a hospital	400	8.5

*Prevalence figures with more than one decimal place were rounded to one decimal place. Abbreviations: SOS: Société Organisation Sociale; EMRO: WHO regional office for the Eastern Mediterranean.

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intervals were 0.0%-4.3% in Somalia, 0.0%-4.1% in Sudan, 0.1%-5.7% in Yemen, and 0.0%-7.0% in this MENA subregion as a whole (Table 3). For the meta-analysis in Yemen, we excluded one study presenting HCV prevalence in a migrant non-Yemeni population [84]. Since only one study was conducted in the general population in Djibouti, no meta-analysis was conducted in this country and the estimate in this study of 0.3% (95%CI: 0.1%-0.4%) was

Table 2. Studies reporting HCV prevalence in high-risk, intermediate-risk and special clinical population groups in Djibouti, Somalia, Sudan and Yemen.

Population risk group	Author, Year	Location	Study period	Study design	Population characteristic	Sample size	Prevalence (%)*
Somalia							
Intermediate-risk	Aceti, 1993 (44)	Mogadishu	1988–1990	Cross-sectional	Hospitalized children at a hospital for diseases other than hepatitis	287	0
	Watts, 1994 (46)	Mogadishu, Merca and Chismayu	1990	Cross-sectional	Female sex workers	236	1.7
	Groen, 2000 (45)	Mogadishu	1995	Cross-sectional	Hospitalized children for measles, tuberculosis, anaemia and other febrile illnesses	42	2.4
	Watts, 1994 (46)	Mogadishu, Merca and Chismayu	1990	Cross-sectional	Patients with STDs	80	2.5
	Groen, 2000 (45)	Mogadishu	1995	Cross-sectional	Hospitalized adult for tuberculosis, malaria, acute respiratory infections, and unknown diagnosis (no clinically evident case of hepatitis)	57	7
Special Clinical populations	Aceti, 1993 (44)	Mogadishu	1988–1990	Cross-sectional	Patients with CLD	110	14.5
	Bile, 1993 (47)	Mogadishu	1989	Case-control	Cases with CLD including HCC	62	40.3
Mixed populations	Aceti, 1993 (44)	Mogadishu	1988–1990	Cross-sectional	Mixed population with high prevalence of <i>Schistosoma haematobium</i> : 98 prisoners and 81 patients from the Psychiatric Clinic of Mogadishu	179	2.2
Sudan							
High risk	Mudawi, 2007b (51)	Khartoum	2001	Cross-sectional	Patients with hepatosplenic schistosomiasis	176	4.5
	Gasim, 2012 (55)	Khartoum	2010	Cross-sectional	Haemodialysis patients	353	8.5
	Gadour, 2011 (53)	Khartoum	2008	Cross-sectional	Patients (males) with haemophilia	62	13
	El-Amin, 2007 (54)	Khartoum	2005	Cross-sectional	Haemodialysis patients	236	23.7
	Mohamedani, 2014 (50)	Gezira	-	Cross-sectional	Patients with schistosomiasis	106	31.1
	Suliman, 1995 (56)	Khartoum	1994	Cross-sectional	Haemodialysis patients	46	34.9
Mixed populations	Mudawi, 2007a (52)	Gezira	2000	Cross-sectional	Participant enrolled from the population of Um Zukra village (population schistosomiasis prevalence of 70%)	410	2.2
Intermediate-risk	IBBS National Team, 2013 (57)	Gezira	2011–2012	Cross-sectional	Female sex workers	296	0
	IBBS National Team, 2013 (57)	Khartoum	2011–2012	Cross-sectional	Men who have sex with men	292	0
	El-Amin, 2007 (54)	Khartoum	2005	Cross-sectional	Employees at a haemodialysis centre	62	0
	IBBS National Team, 2013 (57)	North Kodofan	2011–2012	Cross-sectional	Female sex workers	296	0
	Nail, 2008 (58)	Omdurman	2007	Cross-sectional	Health care workers at the Tropical Diseases Teaching Hospital	211	0
	IBBS National Team, 2013 (57)	River Nile	2011–2012	Cross-sectional	Female sex workers	291	0

(Continued)

Table 2. (Continued)

Population risk group	Author, Year	Location	Study period	Study design	Population characteristic	Sample size	Prevalence (%)*
	IBBS National Team, 2013 (57)	Sinnar	2011–2012	Cross-sectional	Men who have sex with men	312	0
	IBBS National Team, 2013 (57)	White Nile	2011–2012	Cross-sectional	Female sex workers	288	0
	IBBS National Team, 2013 (57)	North Kodofan	2011–2012	Cross-sectional	Men who have sex with men	304	0.2
	IBBS National Team, 2013 (57)	Sinnar	2011–2012	Cross-sectional	Female sex workers	303	0.2
	IBBS National Team, 2013 (57)	Alshamalia	2011–2012	Cross-sectional	Men who have sex with men	305	0.5
	IBBS National Team, 2013 (57)	Khartoum	2011–2012	Cross-sectional	Female sex workers	305	0.5
	IBBS National Team, 2013 (57)	West Darfur	2011–2012	Cross-sectional	Female sex workers	303	0.5
	IBBS National Team, 2013 (57)	River Nile	2011–2012	Cross-sectional	Men who have sex with men	300	0.6
	IBBS National Team, 2013 (57)	Gezira	2011–2012	Cross-sectional	Men who have sex with men	135	1
	IBBS National Team, 2013 (57)	White Nile	2011–2012	Cross-sectional	Men who have sex with men	307	1.1
	IBBS National Team, 2013 (57)	Alshamalia	2011–2012	Cross-sectional	Female sex workers	305	1.5
	Mudawi, 2014 (59)	Khartoum	2010–2012	Cross-sectional	Patients with HIV	358	1.7
	IBBS National Team, 2013 (57)	North Darfur	2011–2012	Cross-sectional	Female sex workers	303	2.6
	McCarthy, 1994 (60)	Juba	1989	Cross-sectional	Paediatric and adolescent patients	666	3
	IBBS National Team, 2013 (57)	South Darfur	2011–2012	Cross-sectional	Female sex workers	299	5.1
	Suliman, 1995 (56)	Khartoum	1994	Cross-sectional	Health care workers at the Khartoum Kidney Dialysis Center	37	5.4
	IBBS National Team, 2013 (57)	South Darfur	2011–2012	Cross-sectional	Men who have sex with men	172	5.9
Special Clinical populations	Ahmed, 2008 (62)	Khartoum	2007	Cross-sectional	Pregnant women with acute viral hepatitis at three main hospitals in Khartoum	16	6.3
	Omer, 2001 (61)	Khartoum	1996–1998	Case-control	Patients with HCC	115	11
Yemen							
High-risk	Haidar, 2002 (68)	Hajjah	1997–1999	Cross-sectional	Haemodialysis patients	30	40
	Aman, 2015 (70)	Aden	2000–2013	Cross-sectional	Haemodialysis patients	219	40.2
	Selm, 2010 (69)	Aden	2007	Case-control	Haemodialysis patients	51	62.7
Intermediate-risk	Haidar, 2002 (68)	Hajjah	1997–1999	Cross-sectional	Hospital employees	200	0.5
	Al-Jarba, 2003	Aden	-	Cross-sectional	Hospital employees: 298 nurses, 95 doctors, 86 technical staff, 55 administrators and 43 maintenance staff	576	1.3
	Shidrawi, 2004 (71)	Sana'a	-	Cross-sectional	Health care workers	546	3.5

(Continued)

Table 2. (Continued)

Population risk group	Author, Year	Location	Study period	Study design	Population characteristic	Sample size	Prevalence (%)*
Special Clinical populations	Gunaid, 1997 (74)	-	-	Cross-sectional	Patients with acute viral hepatitis	78	6.4
	Bakhubaira, 2009 (81)	Aden	2007–2008	Retrospective	Patients with breast cancer, gastrointestinal malignancies and lymphomas	449	8
	Haidar, 2002 (68)	Hajjah	1997–1999	Cross-sectional	Patients suspected to have liver disease	749	8.8
	Salem, 2009 (78)	Sana'a	2005–2007	Case-control	Cases with NHL (females) treated in the haematology and oncology unit (patients coming from different parts of the country)	75	10.7
	Al-Mansoob, 2013 (75)	Sana'a	2009–2011	Cross-sectional	Patients in surgical departments	394	14.2
	Salem, 2009 (78)	Sana'a	2005–2007	Case-control	Cases with NHL (males) treated in the haematology and oncology unit (patients coming from different parts of the country)	117	17.6
	Selm, 2010 (69)	Aden	2007	Cross-sectional	Patients with HCC, CLD, and cirrhosis	67	17.9
	Denis, 1994 (73)	-	1988–1990	Case-control	Cases with leprosy	117	21
	El Guneid, 1993 (80)	Taiz, Sana'a	-	Cross-sectional	Patients with CLD	107	21.8
	Saeed, 2012 (77)	Sana'a	2008–2010	Cross-sectional	Patients with HCC	88	28.4
	Al-Selwi, 2009 (82)	Sana'a	2004–2007	Cross-sectional	Patients with HCC	54	37
	Al-Moslih, 2001 (76)	Sana'a	-	Case-control	Cases with acute and CLD (liver disease, acute viral hepatitis, chronic viral hepatitis, and cryptic or autoimmune disease)	286	37.1
	Salem, 2012 (79)	Sana'a	2001–2008	Cross-sectional	Patients with HCC (with cirrhosis in 187 patients and non-cirrhosis in 64 patients)	251	38.2

*Prevalence figures with more than one decimal place were rounded to one decimal place.

Abbreviations: CLD: chronic liver disease; HCC: hepatocellular carcinoma; NHL: non-Hodgkin lymphomas; STD: sexually transmitted disease; IBBS: integrated bio-behavioural HIV surveillance surveys.

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taken as the estimate for the national population-level HCV prevalence. The forest plots of the country-specific meta-analyses in the general population can be found in Fig 2.

Since the number of studies was less than five in some of the risk categories, meta-analyses were not conducted for all risk categories of all countries. Meta-analyses showed a high mean estimate of HCV prevalence in high-risk populations in Sudan at 14.3% (95%CI: 6.2%-24.9%), and in special clinical populations in Yemen at 19.4% (95%CI: 13.9%-26.0%) (Table 3 and S1 Fig). However, the mean estimates of HCV prevalence were low in intermediate-risk populations in Somalia and Sudan, at 1.7% (95%CI: 0.0%-4.9%) and 0.6%, (95%CI: 0.2%-1.1%), respectively (Table 3 and S1 Fig).

There was significant evidence for heterogeneity in effect size in all meta-analyses (Q-test p -value <0.10) (Fig 2 and Table 3). I^2 heterogeneity measure was high in most meta-analyses, and often exceeded 90%, indicating that most of the variation was attributed to variation in

Table 3. Pooled mean HCV prevalence and meta-analysis summary statistics by risk population in Djibouti, Somalia, Sudan and Yemen.

	Number of studies	Total sample size	Prevalence range (%) [*]	Effect size		Heterogeneity		
				Mean prevalence (%)	Confidence interval (95%)	Q (p-value)	I ² (confidence interval)	Prediction interval (95%)
Djibouti								
High-risk groups	0	0	-	-	-	-	-	-
Intermediate-risk groups	0	0	-	-	-	-	-	-
Special clinical populations	0	0	-	-	-	-	-	-
General population	1	8,057	0.3	-	0.1–0.4	-	-	-
Somalia								
High-risk groups	0	0	-	-	-	-	-	-
Intermediate-risk groups	5	702	0.0–7.0	1.7	0.0–4.9	17.3 (0.002)	77% (44%-90%)	0.0–18.2
Special clinical populations	2	172	14.5–40.3	-	-	-	-	-
General population	9	14,081	0.0–6.5	0.9	0.3–1.9	24.0 (0.002)	67% (32%-83%)	0.0–4.3
Sudan								
High-risk groups	6	979	4.5–34.8	17.3	8.6–28.2	74.6 (<0.0001)	93.3% (88%-96%)	0.0–60.9
Intermediate-risk groups	23	6,450	0.0–5.4	0.6	0.4–0.8	103.5 (<0.0001)	79% (69%-86%)	0.0–4.3
Special clinical populations	2	131	6.3–11.0	-	-	-	-	-
General population	7	1,856	0.0–4.1	1.0	0.3–1.9	12.9 (0.045)	53% (0%-80%)	0.0–4.1
Yemen								
High-risk groups	3	300	40.0–62.7	-	-	-	-	-
Intermediate-risk groups	3	1,322	0.5–3.5	-	-	-	-	-
Special clinical populations	13	2,832	6.4–38.2	19.4	13.0–26.6	231.8 (<0.001)	95% (93%-96%)	0.9–51.8
General population [*]	24	48,343	0.0–8.5	1.9	1.4–2.6	345.3 (<0.001)	93% (91%-96%)	0.1–5.7
All countries								
High-risk groups	9	1,279	4.5–62.7	26.2	14.8–39.4	188.3 (<0.0001)	95% (94%-97%)	0.0–76.1
Intermediate-risk groups	31	8,474	0.0–7.0	0.7	0.3–1.3	139.5 (<0.001)	79% (71%-85%)	0.0–4.7
Special clinical populations	17	3,135	6.4–38.2	19.6	13.9–26.0	253.0 (<0.001)	94% (92%-96%)	1.4–50.2
General population [*]	41	72,337	0.0–8.5	1.5	1.0–2.2	1147.9 (<0.001)	96% (96%-97%)	0.0–7.0

^{*}In the general population of Yemen, one study was not included in the meta-analysis as it reported HCV prevalence in a migrant non-Yemeni population.

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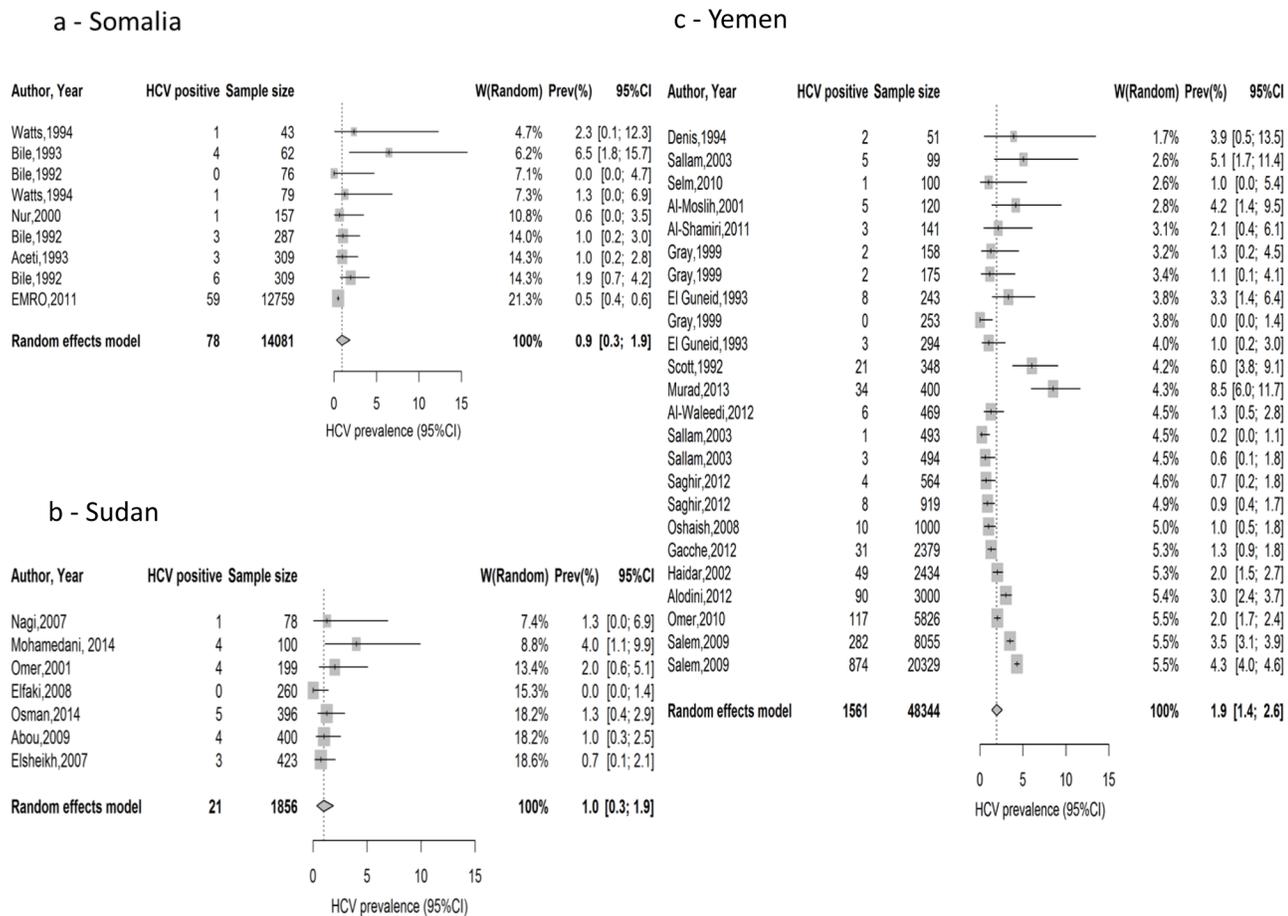


Fig 2. Forest plots presenting the outcomes of the meta-analyses of HCV prevalence studies in the general population in Somalia, Sudan and Yemen.

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effect size across studies rather than chance. The estimated prediction intervals for the pooled means in most analyses were wide suggesting heterogeneity with substantial variation in effect size across individual studies.

Meta-regression

In the multivariable model adjusting for country, subpopulation within the low risk population, study design, study site, and study precision, the meta-regression did not identify any statistically significant prevalence-modifiable factors apart from country. Both Somalia and Sudan had statistically significantly lower HCV prevalence than Yemen. Relative to Yemen, the prevalence in Somalia was lower with an odds ratio (OR) = 0.44; 95%CI: 0.20–0.96; *p*-value = 0.040. Also relative to Yemen, the prevalence in Sudan was lower with an OR of = 0.39; 95%CI: 0.19–0.82; *p*-value = 0.015. Since there was only one prevalence measure for Djibouti, there was not sufficient statistical power to assess the effect size of this country relative to Yemen.

Sensitivity analyses

A substantial fraction of HCV prevalence studies contributing to the estimates for the national population-level HCV prevalence were among blood donors (41%). The pooled estimates for

the national population-level HCV prevalence, after excluding blood donor data, were 0.9% (95%CI: 0.3%–1.9%) in Somalia, 1.0% (95%CI: 0.3%–1.9%) in Sudan and 1.9% (95%CI: 1.4%–2.6%) in Yemen. There was significant evidence for heterogeneity in effect size in Yemen (p -value <0.001); but the evidence was not significant for Somalia and Sudan.

The pooled estimate in Yemen for the national population-level HCV prevalence, after excluding studies with a sample size lower than 1,000 and published before 2000, was 2.4% (95%CI: 1.6%–3.3%). There was also significant evidence for heterogeneity in effect size (p -value <0.001). This sensitivity analysis was not conducted for Somalia and Sudan. In Somalia, only one study had a sample size greater than 1,000 and was published after 2000 [49]. In Sudan, all studies were published after 2000, but none of them had a sample size greater than 1,000.

Risk of bias and quality assessment of HCV prevalence studies

This systematic review included only studies in which HCV infection was ascertained using biological assays. This implies that all the included studies have at least one assessment domain at low ROB (S3 and S4 Tables). In the two other assessment domains, proportion of studies with low ROB was 23% for the sampling methodology and 50% for the response rate. Overall, 100% of studies had at least one assessment domain at low ROB, 51% of the studies had at least two assessment domains at low ROB, and 21% of studies had the three assessment domains at low ROB. Meanwhile, 74% of studies had high ROB in at least one assessment domain, 8% of studies had high ROB in at least two assessment domains, and none of the studies had high ROB in all three assessment domains. In terms of precision of estimates, 78% of studies had good precision (S3 and S4 Tables).

HCV genotypes

This systematic review identified only one and small study describing HCV genotypes [51]. HCV genotype 4 (subtypes e and c/d) was detected in four RNA positive patients out of eight HCV antibody positive cases. These individuals were from a cohort of patients with hepatosplenic schistosomiasis in Khartoum, Sudan.

Risk factors for HCV infection

Crude (unadjusted) and adjusted risk factors for HCV infection were reported in some of included studies. Multivariable analysis was conducted in only a fraction of studies that reported risk factors. The reported unadjusted risk factors included duration of dialysis [54–56]; history of surgical procedures [54, 75, 85, 86], blood transfusion [75, 83, 85], renal transplantation [54, 65], invasive procedures [75], travel abroad [75], blood donation [83] or jaundice [47]; age [54, 93]; education level [85, 93]; gender [78]; use of khat [47]; level of aminotransferases and alfa-fetoprotein [47] and low parity [85]. The reported adjusted risk factors (after adjustment for confounders) included duration of dialysis [55] and history of blood transfusion [83], blood donation [83] and surgery [86]. Furthermore, HCV infection was significantly associated with HCC [61] and CLD [80] in unadjusted analyses and with NHL [78] in an adjusted analysis.

Discussion

Building on a developed and refined methodology [7–9, 12–14], we conducted a systematic review and synthesis of HCV prevalence and its epidemiology in Djibouti, Somalia, Sudan, and Yemen. We also presented estimates for the national population-level HCV prevalence and for

the prevalence among various at risk categories. The results suggest that national population-level HCV prevalence is at about 1% in Somalia, Sudan, and probably Djibouti, but seems twice as high in Yemen at about 2%. High prevalence estimates were identified in these countries among clinical populations at high risk of infection such as HD and haemophilia patients. Notably, we could not identify any study among PWID in this subregion, a key population at high risk of HCV exposure.

HCV prevalence at the national level in these countries is broadly consistent with the levels observed globally [3, 4] and in the MENA region [7, 10–14]. Our estimates nonetheless contrast with earlier work that suggested higher prevalence in these countries [94, 95]. The estimated infection levels are also substantially lower than those found in Egypt at 14.7% [7, 96] and in Pakistan at 4.7% [97, 98]; the two countries with the highest HCV prevalence in MENA. Yemen appears however to have the third highest HCV prevalence in MENA based on the completed and ongoing analyses of the MENA HCV Epidemiology Synthesis Project [7, 10–14]. This highlights the need to improve our understanding of the epidemiology of HCV in this country, a populous country of 27 million people [99] and ongoing military conflict.

A substantial fraction of HCV prevalence studies in the general population were among blood donors. This population category is biased towards healthy populations and may not necessarily be representative of the wider general population. Accordingly our estimates for HCV prevalence in the general population could underestimate actual prevalence [100, 101]. HCV prevalence could in principle be declining due to population growth combined with a reduction in exposure following the global introduction in the 1990s of more stringent blood screening and infection control protocols. We conducted two sensitivity analyses to examine the impact of excluding blood donors studies and older than 2000 studies on our estimates. The sensitivity analyses indicated a small impact on our estimates for Somalia and Sudan, but suggested that we may be underestimating HCV prevalence in Yemen. Estimated HCV prevalence in Yemen increased from 1.9% in our baseline analysis to 2.8% and 2.4% in the two sensitivity analyses, respectively. These analyses in addition to the meta-regression, therefore affirmed that national population-level HCV prevalence in this subregion of MENA is comparable to global levels, but that Yemen appears to have the third highest HCV prevalence in MENA.

A recent global study by Gower *et al.* has produced an estimate for HCV prevalence in Yemen, but no estimates for HCV prevalence in the other countries of this subregion. The reported estimate by Gower *et al.* is similar to ours (2.2% vs. 1.9%, respectively), however, Gower *et al.* estimate was based on a single study, whereas ours was based on 24 studies [68, 70, 73, 76, 79, 80, 83–93]. The expanded search in our review has allowed us to identify HCV measures published in non-indexed journals and country-level reports. These studies may not have been recognized since they could not be identified using conventional international search engines such as PubMed or Embase. For the same reasons, our study has also identified substantially more HCV data in Somalia and Sudan than recent systematic reviews of HCV prevalence in sub-Saharan Africa [4, 102–104].

Our results suggest ongoing HCV transmission in clinical settings in Djibouti, Somalia, Sudan, and Yemen. This is indicated by the high HCV prevalence in high risk and special clinical populations, regardless of the year of study. Ongoing transmission in clinical settings was also indicated by the significant association between HCV infection and healthcare procedures such as dialysis [55], blood transfusion [83], blood donation [83] and surgery [86]. Ongoing transmission in clinical settings was also suggested by the higher HCV prevalence in intermediate-risk populations, such as hospitalized adults and children and HCWs.

Community transmissions of HCV infection appear to occur in the south-west region of the Arabian Peninsula [83, 105]. In the south-west region of the Kingdom of Saudi Arabia (KSA),

the bordering region of Yemen, HCV transmission was linked to traditional phlebotomy (cupping with blood-letting, known in the Arab world as *hijama*) [105]. The south-west region of KSA presented similar HCV prevalence levels with Yemen and the highest HCV prevalence compared with the other regions in KSA [10]. In Yemen, cupping was significantly associated with increased odds of hepatitis B [83], another blood borne virus sharing transmission routes with HCV through infected blood and needles [106, 107]. As it was observed in Egypt [108] and in Japan [109], folk remedies such as traditional phlebotomy using non-sterilized knives should be considered as possible HCV transmission routes potentially explaining the higher HCV prevalence in Yemen and more broadly in the south-west region of the Arabian Peninsula.

PWID [110–112], prisoners [113] and HIV infected MSM [114] are key contributors to HCV transmission dynamics in both developed and developing countries [113, 115]. We could not identify any study of HCV prevalence among PWID, prisoners, or HIV infected MSM; a major shortcoming of the epidemiological evidence in this subregion. The estimated population proportion of injecting drug use is 0.03% in Somalia, 0.20% in Sudan, and 0.23% in Yemen [116]. The population proportion of injecting drug use in MENA is in the intermediate range compared to global levels at 0.24% [113]. The population proportion of MSM in MENA seems to be consistent with reported global levels of 2%–3% [117]. Substantial HIV prevalence has already been identified among MSM in MENA such as in Sudan where HIV prevalence was estimated in different studies at 8–9% [117]. Prison population rates were 83, 13.3, 32.5, 56, and 55 per 100,000 of national populations in Djibouti, Somalia, South Sudan, Sudan, and Yemen in 2013 [118]. These estimates suggest the potential existence of large and hidden high risk populations where the level of infection is unknown, but probably substantial given HCV prevalence levels in these high risk populations in other MENA countries [113, 115, 118, 119] and globally [114, 116, 120]. This lack of evidence for PWID, prisoners, and HIV infected MSM makes it difficult to assess the relative importance of these key risk groups as contributors to HCV transmission dynamics in this subregion.

As discussed in details previously [7–14], among the limitations of such systematic review and meta-analyses is the variability in quantity and quality of studies across countries. For instance, only one study was identified for Djibouti, while 44 studies were identified for Yemen. The pooled mean HCV prevalence estimates may have been also affected by selection bias or investigator bias in included studies. The meta-analyses confirmed considerable heterogeneity in effect size across studies, but the sources of variation remain poorly understood. Given the possibility that this heterogeneity may reflect non-random biases, the prediction intervals calculated for each risk population category (Table 3) may provide a more interpretable summary of the variation in effect size and potential true population mean. We classified the populations into different risk categories based on convention in the literature; however, there is no established existing classification of risk for some populations [12]. We classified these based on our best judgment of HCV risk of exposure.

Conclusions

The national population-level HCV prevalence is at about 1% in Somalia, Sudan, and probably Djibouti, and is comparable to most countries in MENA and globally. However, HCV prevalence in Yemen appears to be at a higher level, at about 2%, making Yemen the country with the third highest HCV prevalence in MENA based on the MENA HCV Epidemiology Synthesis Project analyses [7, 10–13, 121]. The high HCV prevalence found among different clinical populations suggests ongoing HCV transmission in clinical settings. This points out the need to implement strict measures to prevent HCV transmission such as improved injection safety

and properly screened blood transfusions [122, 123]. Establishment of HCV treatment programs should also be explored given the increasing availability and affordability of the new antiviral treatments and generics to cure HCV infection [124–126].

Strikingly, we could not identify any study among PWID, prisoners or HIV infected MSM, a major shortcoming of the epidemiological evidence in this subregion. The contributions of these populations to HCV incidence and prevalence remain unknown. An improved understanding of the epidemiology of HCV infection in this subregion is warranted; this resource-limited subregion remains the least studied subregion in MENA. Improved understanding can be achieved by conducting representative surveys among at risk populations as well as nationally-representative population-based surveys to estimate infection and disease occurrence, geographic variability, modes of exposure, and HCV knowledge and attitudes, as has been done recently in other MENA countries such as Egypt [6, 127–131].

Supporting Information

S1 Fig. Forest plots presenting the outcomes of the meta-analyses of HCV prevalence studies among intermediate risk groups in Somalia and Sudan, special clinical populations groups in Yemen, and high risk groups in Sudan.

(TIF)

S1 Table. PRISMA 2009 Checklist.

(PDF)

S2 Table. Search criteria for the systematic review of HCV antibody prevalence in Djibouti, Somalia, Sudan, and Yemen.

(PDF)

S3 Table. Study-level assessment of precision and risk of bias in HCV antibody prevalence measures, as extracted from eligible reports.

(PDF)

S4 Table. Summary of study-level assessment of precision and risk of bias in HCV antibody prevalence measures, as extracted from eligible reports.

(PDF)

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Author Contributions

Conceived and designed the experiments: KC LJA-R. Performed the experiments: KC. Analyzed the data: KC SPK. Wrote the paper: KC LJA-R.

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