



Epidemiology of hepatitis C virus in the WHO Eastern Mediterranean Region:

implications for strategic action

Epidemiology of hepatitis C virus in the WHO Eastern Mediterranean Region:

implications for strategic action

WHO Library Cataloguing in Publication Data

Names: World Health Organization. Regional Office for the Eastern Mediterranean

Title: Epidemiology of hepatitis C virus in the WHO Eastern Mediterranean Region: implications for strategic action / World Health Organization. Regional Office for the Eastern Mediterranean

Description: Cairo: World Health Organization. Regional Office for the Eastern Mediterranean, 2020

Identifier: ISBN 978-92-9274-435-9 (pbk.) | ISBN 978-92-9274-436-6 (online)

Subjects: Hepatitis C - epidemiology | Hepatitis C - prevention & control | Hepacivirus | Eastern Mediterranean Region

Classification: NLM WC 536

This publication was originally published under ISBN 978-92-9022-285-9, 978-92-9022-286-6

© World Health Organization 2020

Some rights reserved. This work is available under the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 IGO licence (CC BY-NC-SA 3.0 IGO; <https://creativecommons.org/licenses/by-nc-sa/3.0/igo>).

Under the terms of this licence, you may copy, redistribute and adapt the work for non-commercial purposes, provided the work is appropriately cited. In any use of this work, there should be no suggestion that WHO endorses any specific organization, products or services. The use of the WHO logo is not permitted. If you adapt the work, then you must license your work under the same or equivalent Creative Commons licence. If you create a translation of this work, you should add the following disclaimer along with the suggested citation: "This translation was not created by the World Health Organization (WHO). WHO is not responsible for the content or accuracy of this translation. The original English edition shall be the binding and authentic edition".

Any mediation relating to disputes arising under the licence shall be conducted in accordance with the mediation rules of the World Intellectual Property Organization.

Suggested citation. Epidemiology of hepatitis C virus in the WHO Eastern Mediterranean Region: implications for strategic action. Cairo: WHO Regional Office for the Eastern Mediterranean; 2020. Licence: CC BY-NC-SA 3.0 IGO.

Sales, rights and licensing. To purchase WHO publications, see <http://apps.who.int/bookorders>. To submit requests for commercial use and queries on rights and licensing, see <http://www.who.int/about/licensing>.

Third-party materials. If you wish to reuse material from this work that is attributed to a third party, such as tables, figures or images, it is your responsibility to determine whether permission is needed for that reuse and to obtain permission from the copyright holder. The risk of claims resulting from infringement of any third-party-owned component in the work rests solely with the user.

General disclaimers. The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by the World Health Organization in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

All reasonable precautions have been taken by the World Health Organization to verify the information contained in this publication. However, the published material is being distributed without warranty of any kind, either expressed or implied. The responsibility for the interpretation and use of the material lies with the reader. In no event shall the World Health Organization be liable for damages arising from its use.

Contents

iv Acknowledgements

v Executive summary

01 Introduction

04 Research methodology and conceptual framework

08 Hepatitis C virus (HCV) epidemiology among populations with high risk health care exposure to HCV and populations with liver-related conditions

19 HCV epidemiology among people who inject drugs

26 HCV epidemiology among populations at intermediate risk of exposure to HCV

33 HCV epidemiology among the general population

40 Modes of exposure to HCV infection in the WHO Eastern Mediterranean Region

44 Analytical insights into HCV transmission dynamics in the WHO Eastern Mediterranean Region

47 Responding to viral hepatitis with a focus on HCV infection across the WHO Eastern Mediterranean Region: the way forward

51 References

Acknowledgements

This report was drafted based on a series of scientific studies to characterize hepatitis C virus epidemiology in the Eastern Mediterranean Region. The following authors contributed to drafting of the report:

Infectious Disease Epidemiology Group, Weill Cornell Medicine-Qatar, Cornell University:

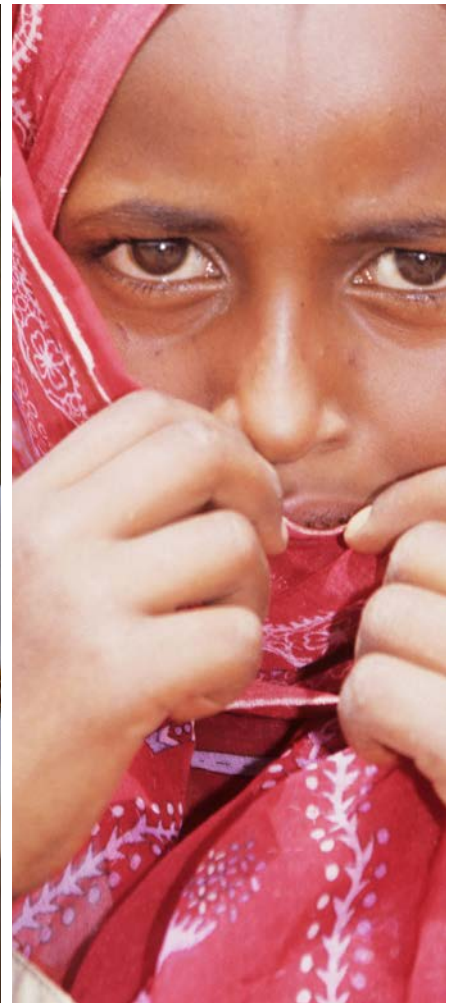
Hiam Chemaitelly (lead author), Sarwat Mahmud, Karima Chaabna, Silva P. Kouyoumjian, Ghina Mumtaz, and Laith J. Abu-Raddad (principal investigator).

World Health Organization:

Gabriele Riedner and Joumana Hermez.

This report was reviewed and benefited from valuable comments by Dr Yvan Hutin (World Health Organization) and Professor Nico Nagelkerke (Erasmus University).

This report was supported by the World Health Organization Regional Office for the Eastern Mediterranean. The original scientific research that formed the basis of this report was conducted with generous funding from the Qatar National Research Fund (a member of Qatar Foundation) through NPRP grant numbers 4-924-3-251 and 9-040-3-008. The statements made herein are solely the responsibility of the authors. Infrastructure support was provided by the Biostatistics, Epidemiology, and Biomathematics Research Core at Weill Cornell Medicine-Qatar.



Executive summary

Hepatitis C virus (HCV) is a major cause for liver fibrosis, cirrhosis and cancer and a growing public health concern. HCV is estimated to affect about 1% of the population in most countries globally leading to about 71 million prevalent chronic infections and causing about 400 000 deaths every year. Most of HCV transmission is bloodborne and is largely preventable. To address this global health challenge, the World Health Organization (WHO) has recently formulated the Global health sector strategy on viral hepatitis, 2016–2021 with the aim of reducing, and potentially eliminating, the burden of viral hepatitis infections including HCV. Several tools were further developed by WHO to optimize viral hepatitis surveillance, generate evidence that can effectively inform policy and programming, and monitor progress towards achieving strategic goals for viral hepatitis.

In the WHO Eastern Mediterranean Region, HCV accounts for about two thirds of viral hepatitis morbidity and mortality. Furthermore, in two countries, Egypt and Pakistan, HCV antibody (Ab) prevalence is substantially higher than global levels. Achieving the goals outlined by the Global health sector strategy on viral hepatitis, 2016–2021 requires, as a foundation, a comprehensive assessment of HCV infection epidemiology in the Region to inform public health policy and programming and to ensure adequate allocation of resources.

This report presents results and findings of the Eastern Mediterranean Region HCV Epidemiology Synthesis Project which aimed to characterize HCV epidemiology across countries through comprehensive systematic reviews and synthesis of published and unpublished HCV epidemiological measures in the Region. The report provides an analytical description of HCV epidemiology among the different populations at risk of acquiring the infection, discusses risk factors and major drivers of HCV transmission, and estimates HCV-Ab prevalence among the various populations at risk of HCV infection for each country in the Region. All countries of the Region were

included in this project, namely Afghanistan, Bahrain, Djibouti, Egypt, Islamic Republic of Iran, Iraq, Jordan, Kuwait, Lebanon, Libya, Morocco, Oman, Pakistan, Palestine, Qatar, Saudi Arabia, Somalia, Sudan, Syrian Arab Republic, Tunisia, the United Arab Emirates and Yemen.

The HCV Epidemiology Synthesis Project followed a rigorous and standardized study methodology. HCV epidemiological measures were identified through systematic reviews of thousands of data sources following Cochrane Collaboration guidelines. The population in the Region was classified into four population groups according to their risk of acquiring HCV infection: 1) populations with high risk health care exposure to HCV (at risk of acquiring HCV infection due to a medical condition that requires frequent injections or blood transfusions); 2) people who inject drugs (PWID); 3) populations at low risk of infection (general population); 4) populations at intermediate risk of infection (people with a higher risk of infection than the general population but lower than populations with high risk health care exposure and PWID). We also assessed HCV infection levels among populations with liver-related conditions given their relevance for understanding the epidemiology of HCV infection. Meta-analyses were conducted to estimate HCV-Ab prevalence for the different populations at risk for each country.

High incidence of HCV infection has been reported in the Region among populations with high risk health care exposure. HCV-Ab prevalence was also high among these populations with about half of the studies reporting levels exceeding 28% among haemodialysis, thalassaemia and haemophilia patients. These findings suggest ongoing HCV transmission due to less than optimal infection control procedures in health care settings. High HCV-Ab prevalence was also observed among populations with liver-related conditions, among whom the median HCV-Ab prevalence varied between 7% for acute viral hepatitis patients and 52% for hepatocellular carcinoma patients. These prevalence levels indicate that HCV infection is a

major cause of the liver disease burden in the Region.

There are over half a million PWID in the Region, about 15 PWID for every 10 000 adults in the population. PWID in the Region engage in high levels of injecting risk behaviour with about half of them reporting ever sharing a needle/syringe and about a quarter reporting sharing a needle/syringe during the last injection. The mean HCV-Ab prevalence among this population was estimated at 45% across the Region, which is comparable to global levels. However, HCV-Ab prevalence exceeding 70% has been reported among PWID in several countries – Afghanistan, Islamic Republic of Iran, Libya, Pakistan, and Saudi Arabia.

Among populations at intermediate risk of exposure to HCV infection in the Region, HCV-Ab prevalence was about 4%, higher than that observed among the general population, but substantially lower than that observed among populations with high risk health care exposure to HCV and PWID. However, some intermediate risk populations have higher HCV-Ab prevalence levels, such as patients with diabetes (15%), household contacts of HCV-infected patients (11%), and barbers (5%), suggesting the potential for household and community-related exposures to HCV infection. High HCV-Ab prevalence was also reported among prisoners, possibly due to high risk behaviours, such as injecting drug use during or before incarceration, tattooing, piercing, unprotected anal sex and sharing of infected personal items.

Egypt and Pakistan are the countries most affected by HCV infection in the Region with a national HCV-Ab prevalence of about 10% and 5%, respectively. For the rest of the countries, HCV-Ab prevalence among the general population is below 3%, and most often in the range of 1%, which is comparable to global levels. A few studies estimated incidence of HCV infection among general population groups. All but one were conducted in Egypt and showed considerable rates of HCV infection suggesting substantial ongoing transmission of HCV infection.

HCV infection transmission in the Region appears to be primarily driven by less than optimal infection control in health care settings. Specific risk factors repeatedly implicated in exposure to HCV infection include haemodialysis, blood transfusion, surgery, injections, dental procedures, and contaminated medical equipment. HCV transmission in the Region appears also to occur through informal health care exposure in the community, for example through the use of unsterile needles/syringes for medical injections and the use of contaminated sharp objects for minor surgical procedures such as blood-letting (hijama) and circumcision. HCV is also transmitted through mother-to-child transmission which is an important contributor to rates of HCV infection in Egypt

and also possibly in Pakistan, but is unlikely to be so in other countries because of the lower HCV-Ab prevalence among women of reproductive age.

With the exception of hepatitis B virus childhood vaccination, programmes to control viral hepatitis have not received due attention in most countries. Screening and case detection of chronic HCV infection continues to be low even in countries where viral hepatitis programmes are in place. Ensuring access to care and treatment services, including treatment with direct-acting antivirals for HCV, remains a major challenge across the Region with high treatment costs a key obstacle. The protracted emergencies in several countries have also slowed and complicated the scale-up of viral hepatitis efforts.

Eliminating viral hepatitis in the Region requires each country to set its own evidence-informed national response to effectively achieve prevention of new infections, treatment of chronic infections and control of hepatitis disease sequelae. Based on the *WHO Global health sector strategy on viral hepatitis, 2016–2021*, the WHO Regional Office for the Eastern Mediterranean has developed a *Regional action plan for the implementation of the Global health sector strategy for viral hepatitis 2017–2021* to guide Member States and the WHO Secretariat on priority actions towards the achievement of national, regional and global targets for viral hepatitis. The regional action plan will be implemented in a phased manner with different starting points for different countries depending on the status of the response to viral hepatitis in 2016. If adopted and implemented by each country, the regional action plan will result in tangible progress towards the global goal of eliminating HCV and hepatitis B virus infections by 2030.

1

Introduction





1 Introduction



Viral hepatitis has been identified as a leading cause of death globally based on data from the Global Burden of Disease Study, superseding human immunodeficiency virus (HIV), tuberculosis and malaria (1).

Nearly half of this mortality is attributed to hepatitis C virus (HCV) and the disease burden caused by this virus is a growing public health concern (1). Infection with HCV, a virus that was characterized only in 1989 (2,3), causes acute hepatitis, fibrosis, cirrhosis and liver cancer among other forms of disease (4,5). HCV is estimated to affect about 1% of the population in most countries globally with about 71 million prevalent chronic infections and causing about 400 000 deaths every year (4,5).

Upon HCV infection, 20–30% of infected individuals showing symptoms which are often mild (6–9). About a quarter of infected individuals clear the infection spontaneously, while the rest progress to chronic HCV infection and become HCV RNA positive and HCV antibody (Ab) positive. Chronically infected individuals are at risk of developing extrahepatic manifestations and of progressing to liver fibrosis. About 15–30% of chronically infected persons further develop compensated and decompensated cirrhosis within 20 years (7,8). Hepatocellular carcinoma can also develop at a risk of 1–3% within 30 years (9). HCV diagnostic tests have improved immensely over the years for both HCV antibodies and HCV RNA, and have very high sensitivity and specificity, particularly since the introduction of third and fourth generation assays for antibody testing (10).

Most of HCV transmission is bloodborne and is largely preventable (11,12). Common modes of transmission include transfusion of infected blood or blood-related products, use of contaminated medical equipment, sharing of unsterile needles and syringes, and mother-to-child transmission (13,14). While interventions targeting

HCV mostly focused on infection control in the past, the recent breakthroughs in HCV treatment, namely the highly efficacious oral direct-acting antiviral therapy, have opened new opportunities for controlling HCV infection, reducing the burden and cost of managing liver-related conditions, and even eliminating this virus as a public health concern (15).

Considering this global health challenge, the World Health Organization (WHO) has formulated the Global health sector strategy on viral hepatitis, 2016–2021 (16). The strategy provides countries with guidance on reducing, and potentially eliminating, the burden of viral hepatitis infections (16,17). Specifically, the strategy advocates for combining treatment with prevention and for adopting a test and treat approach to achieve elimination of viral hepatitis as a major public health problem by 2030 (16,17). In line with this strategy, several tools were developed to support the set-up and expansion of national hepatitis plans and/or programmes, optimize the surveillance of viral hepatitis including HCV, and generate strategic information that can effectively inform prevention, control and treatment policies and programmes (18,19). Progress towards achieving the strategic goals for viral hepatitis will be monitored for each country through a set of indicators that convey essential information on the national response to viral hepatitis, and on temporal trends in infection levels and related mortality (20).



While HIV programmes in the WHO Eastern Mediterranean Region have considerably progressed in recent years, programmes targeting HCV infection are still lagging in most countries despite evidence that North Africa and the Middle East is the region most affected by HCV infection (1). Roughly two thirds of viral hepatitis mortality in North Africa and the Middle East, which is the fifth leading cause of death in this region, is attributed to HCV infection (1). HCV infection also accounts for 57% of disability-adjusted life-years (DALYs) due to viral hepatitis (1). A few countries appear to be most affected by HCV, namely Egypt and Pakistan, where the national HCV-Ab prevalence has been assessed at about 10%¹ (21–23) and 5% (24,25), respectively. Meanwhile, prevalence levels remain poorly estimated for the rest of the countries of the Region. Achieving the goals outlined by the Global health sector strategy on viral hepatitis requires, as a foundation, a comprehensive assessment of the epidemiology of HCV infection in the Region to inform public health policy and programmes and to ensure adequate allocation of resources.

Against this background, this report presents the results and findings of the Eastern Mediterranean Region HCV Epidemiology Synthesis Project, which aimed to characterize HCV epidemiology across countries of the Region through comprehensive systematic reviews and synthesis of published and unpublished HCV epidemiological measures. The report provides an analytical description of HCV infection epidemiology among the different populations at risk of acquiring the infection, discusses risk factors and major drivers of HCV transmission, and assesses HCV-Ab prevalence among the various populations at risk of HCV infection for each country. The ultimate goal of this synthesis is to provide the scientific evidence necessary for strategic prioritization, resource allocation and effective interventions to control HCV infection and its disease burden in the Region. The protocol and evidence generated by this project have been published in a series of studies in the scientific literature (14,22,26–35). This report summarizes the results and findings of these studies from a regional perspective. This work takes heed of recent efforts of WHO highlighting the use of health estimates to inform policy and planning at the country level and promoting the use of standardized methods and tools to generate information for health-related indicators (36).

1. Prevalence of HCV-Ab in the total population in Egypt was estimated using the age-specific prevalence of HCV-Ab as per the 2015 Egypt Demographic and Health Survey for populations aged 1–59 years and the 2008 Egypt Demographic and Health Survey for the population aged 60 years and above. Specifically, we assumed that prevalence of HCV-Ab among the population currently older than 60 years was equal to the prevalence of HCV-Ab among the population that was 54–59 years old during the 2008 Egypt Demographic and Health Survey.

2

Research methodology and conceptual framework

05

- Eastern Mediterranean Region HCV Epidemiology Synthesis Project
- Data sources and search strategy

06

- Data screening and extraction
- Classification of populations and data synthesis

07

- Quantitative analyses
- Methodological limitations

53

- References





2.

Research methodology and conceptual framework

Eastern Mediterranean Region HCV Epidemiology Synthesis Project

The findings of the HCV Epidemiology Synthesis Project are based on an evidence-based epidemiological synthesis and analysis of extensive literature on HCV infection epidemiology using a rigorous and standardized methodology implemented across countries in the Region. The methodology focused on identifying, assessing and analysing HCV infection epidemiological measures to determine HCV infection levels among various at-risk populations and on highlighting modes of exposure to HCV. The overarching goal of this synthesis is to inform health policy, public health programming and resource allocation in the Region. The methodology for this work is briefly described below, however, details of the methodology have been published elsewhere (1–10).

This report focuses on countries of the Eastern Mediterranean Region of WHO. These are: Afghanistan, Bahrain, Djibouti, Egypt, Islamic Republic of Iran, Iraq, Jordan, Kuwait, Lebanon, Libya, Morocco, Oman, Pakistan, Palestine, Qatar, Saudi Arabia, Somalia, Sudan², Syrian Arab Republic, Tunisia, United Arab Emirates and Yemen.

Data sources and search strategy

HCV epidemiological measures were identified through systematic reviews of thousands of data sources following Cochrane Collaboration guidelines (11), and the findings are reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines (12). The surveyed data sources include the following.

1. International scientific databases: PubMed and Embase were searched with no language or year restrictions using broad search criteria with free text terms and medical index terms (MeSH/Emtree) including all subheadings.
2. Regional and country databases and journals: WHO Index Medicus for the Eastern Mediterranean Region, WHO African Index Medicus, the Iraqi Academic Scientific Journals' database, Scientific Information Database of the Islamic Republic of Iran and multiple non-indexed local journals were searched using broad keywords for country name or hepatitis.
3. Abstract archives of non-indexed international conferences: the abstract archives of the International AIDS Society Conference were searched using broad keywords for country names or hepatitis.

2. Available data for Sudan before 2011, the year of independence of South Sudan, may have come from both Sudan and the newly independent Republic of South Sudan.



4. The Middle East and North Africa HIV/AIDS Epidemiology Synthesis Project database: this database includes hundreds of reports of country-level and international organizations. The international organizations that contributed reports include WHO, the United Nations Office on Drugs and Crime (UNODC), the Joint United Nations Programme on HIV/AIDS (UNAIDS), the World Bank, the Office of the United Nations High Commissioner for Refugees (UNHCR), the United Nations Children's Fund (UNICEF), the International Centre for Prison Studies (ICPS), the International Agency for Research on Cancer (IARC), the Population Reference Bureau (PRB) and Family Health International (FHI).

Records were considered for data synthesis and analysis if they were published after 1989, the year when HCV was first characterized (13,14).

Data screening and extraction

The search results were imported into a reference manager, *Endnote*, where duplicate publications were identified and excluded. The titles and abstracts of the remaining records were screened for relevance and the full-texts of relevant or potentially relevant documents were retrieved for further screening. The references of all literature reviews were also checked to identify additional records that could have been potentially missed.

Any record reporting a measure of HCV incidence (new HCV infection) and/or prevalence (existing HCV infection) among populations of countries in the Region was considered (antibody presence provides serological evidence of past or present infection, while, RNA presence provides evidence of HCV infection). Our main focus in this report is on HCV-Ab measures, given the focus on the risk of exposure to HCV infection in this epidemiologically-driven analysis. For each study included, data were extracted on: author(s), complete citation, year(s) of data collection, publication type, country of origin, country of survey, city, study site, study design, sampling technique, study population and its characteristics (sex, age, nationality, etc.), sample size, incidence and/or prevalence along with data related to the ascertainment of the infection, and risk factors for HCV infection. For studies on mother-to-child transmission, data on the level of HCV viraemia among newborns at the end of the follow-up duration of the studies were extracted. All identified HCV incidence

and prevalence measures were included in the analyses; specific selection criteria based on which generation of assay was used were not applied.

The screening and data extraction from documents published in languages other than English were performed by native speakers of the language.

Classification of populations and data synthesis

Populations were classified according to their risk/probability of acquiring HCV infection, as follows.

1. Populations with high risk health care exposure: these include people at risk of acquiring HCV infection due to a medical condition that requires frequent injections or blood transfusions such as haemodialysis, thalassaemia, haemophilia and multi-transfused patients, among others.
2. People who inject drugs (PWID): these include people at risk of acquiring HCV infection due to drug injection.
3. Populations at low risk (general population): these include people who have a low risk of acquiring HCV infection, such as blood donors, pregnant women, healthy children and adults, and individuals undergoing pre-marital or pre-employment blood screening, among other general population groups.
4. Populations at intermediate risk: these include people with an intermediate risk of acquiring the infection, i.e. those with a risk of infection that is higher than the general population but lower than populations with high risk health care exposure and PWID. These populations include health care workers, household contacts of HCV-infected people, hospitalized populations, people with diabetes, men who have sex with men, prisoners and barbers, among others.

We also assessed HCV-Ab prevalence levels among populations with liver-related conditions given their specific relevance for understanding the epidemiology of HCV infection. These include people with chronic liver disease, acute viral hepatitis, hepatocellular carcinoma and liver cirrhosis, among others.



Quantitative analyses

For each country, data on HCV-Ab incidence and prevalence for each population at risk of acquiring the infection (e.g. general population) and subpopulations within these populations (e.g. blood donors, pregnant women) were summarized as relevant using statistical measures including the median HCV-Ab prevalence. An estimate of the mean HCV-Ab prevalence was calculated for each population at risk of acquiring the infection in each country using meta-analyses. The meta-analyses summarized the collective evidence on HCV infection by pooling data from all available studies into one large sample. A minimum of three HCV-Ab prevalence measures was necessary to generate an estimate of the mean HCV-Ab prevalence. Whenever only two studies were available, a mean was calculated using the average of the reported values. The point prevalence was reported for single studies. As there was a paucity of age-stratified studies, age standardization was not done. Each study included in the meta-analysis had to have a minimum of 25 participants. The weighted mean for HCV-Ab prevalence was calculated after weighting the contribution of individual studies using a DerSimonian-Laird random effects model (15). This model accounts for both sampling variation and heterogeneity in measures. The 95% confidence interval (CI) was also calculated around the mean HCV-Ab prevalence.

Methodological limitations

This synthesis is limited by the variability in the quantity and quality of studies across countries. Only a few studies measured HCV-Ab incidence. Reports of HCV-Ab prevalence varied by country, population type, year and geographical location within the country. For example, there were a large numbers of studies on HCV infection in some countries such as Egypt, Islamic Republic of Iran, Pakistan and Saudi Arabia but few studies were available in other countries such as Djibouti. Moreover, while substantial evidence on HCV infection among PWID was available in Afghanistan, Islamic Republic of Iran and Pakistan, a limited amount of data was available for many other countries in the Region.

The quality of the HCV measures synthesized in this study was overall good with the majority of the studies being published in peer-reviewed scientific journals and using assays with acceptable sensitivity and specificity. However, measures of HCV infection based on nationally-representative population-based surveys, which are the gold standard and the most representative of the studied populations, were only available in a few countries. Despite these limitations, all data, irrespective of their representativeness, provided a consistent picture of HCV epidemiology in the Region. The synthesis followed a rigorous methodology that took into account the data limitations in the different analyses.



3

HCV epidemiology among populations with high risk health care exposure to HCV and populations with liver-related conditions

10

- HCV infection incidence among populations with high risk health care exposure to HCV

11

- HCV-Ab prevalence among populations with high risk health care exposure to HCV

13

- Estimates of mean HCV-Ab prevalence among populations with high risk health care exposure to HCV

14

- HCV-Ab prevalence among populations with liver-related conditions

16

- Estimates of mean HCV-Ab prevalence among populations with liver-related conditions

18

- Key highlights

55

- References





3.

HCV epidemiology among populations with high risk health care exposure to HCV and populations with liver-related conditions

Section 3 presents the epidemiological evidence of HCV infection among populations with high risk health care exposure to HCV as well as populations with liver-related conditions across countries. Estimates of HCV-Ab prevalence among these populations in each country are also presented.

The populations with high risk health care exposure includes people at risk of acquiring HCV infection due to a medical condition that requires frequent injections or blood transfusions, such as haemodialysis, thalassaemia, haemophilia, and multitransfused patients, among others. The populations with liver-related conditions include people with chronic liver disease, acute viral hepatitis, hepatocellular carcinoma (liver cancer) and liver cirrhosis.



HCV infection incidence among populations with high risk health care exposure to HCV

Few countries had data on HCV-Ab incidence among populations with high risk health care exposure to HCV (Table 1). These were Egypt, Islamic Republic of Iran, Iraq, Jordan, Morocco and Tunisia. High levels of incidence of

HCV infection were observed across countries with the proportion of people acquiring the infection over different time durations ranging from as low as 4.3% in the Islamic Republic of Iran (1) to as high as 100% in Egypt (2), with a median of 20.8%. High incidence rates in the range of 2.3 to 40.3 per 1 000 person – years were also reported (3–5). These findings indicate ongoing HCV transmission in medical facilities and highlight the need for strengthening infection control programmes, especially in haemodialysis and blood transfusion units across the Region.

Table 1. Studies reporting the incidence of HCV infection among populations with risk health care exposure to HCV in countries of the Region

| First author, year of publication [citation] | Year(s) of data collection | Population | Sample size | HCV seroconversion risk (relative to total sample size) ¹ | Incidence rate (per 1 000 person-years) ² | Duration of follow-up (months) |
|--|----------------------------|---|-------------|--|--|--------------------------------|
| Egypt | | | | | | |
| Zahran, 2014 (2) | | Haemodialysis patients | 44 | 100.0 | | 36.7 |
| Soliman, 2013 (6) | 2008–2010 | Haemodialysis patients following a strict isolation programme | 27 | 14.8 | | 36.0 |
| Soliman, 2013 (6) | 2008–2010 | Haemodialysis patients not following a strict isolation programme | 56 | 42.9 | | 36.0 |
| Khodir, 2012 (7) | 2011–2011 | Haemodialysis patients | 1 527 | 11.0 | | 8.0 |
| El-Sherif, 2012 (8) | | Haemodialysis patients | 14 | 21.4 | | 4.0 |
| Goher, 1998 (9) | | Haemodialysis patients on non-reused dialysis machines | 37 | 21.6 | | 6.0 |
| Goher, 1998 (9) | | Haemodialysis patients on reused dialysis machines | 53 | 20.8 | | 6.0 |
| Islamic Republic of Iran | | | | | | |
| Jabbari, 2008 (1) | 2005–2006 | Haemodialysis patients | 70 | 4.3 | | |
| Azarkeivan, 2012 (10) | 1996–2009 | Thalassaemia patients | 307 | 6.8 | | |
| Iraq | | | | | | |
| Al-Rubaie, 2011 (3) | 2009 | Haemodialysis patients | | 57.0 | 40.3 | 12.0 |
| Jordan | | | | | | |
| Batieha, 2007 (11) | 2003 | Haemodialysis patients | 1 300 | 9.2 | | 12.0 |
| Morocco | | | | | | |
| Sekkat, 2008 (4) | 2003–2004 | Haemodialysis patients | | | 9.4 | |
| Tunisia | | | | | | |
| Ben Othman, 2004 (5) | 2000–2002 | Haemodialysis patients | | | 2.3 | |

1. Proportion of people who acquired the infection during the follow-up duration of the study.

2. Number of people who acquired the infection over the total duration of follow-up for all participants in the study.



HCV-Ab prevalence among populations with high risk health care exposure to HCV

Hundreds of studies have been conducted among populations with high risk health care exposure to HCV in the Region (Fig. 1). These studies showed high HCV-Ab prevalence levels with most studies reporting prevalence measures well above 10%. About half of the studies reported HCV-Ab prevalence measures greater than 28.1%.

Studies further show that the high HCV-Ab levels are not limited to a specific population group, such as multitransfused patients, but are found across the different population groups at high risk of health care exposure (Fig. 2). For instance, HCV-Ab prevalence ranged from 2.3% to 100% with a median of 49% among haemophilia patients, from 0% to 98% with a median of 29% among haemodialysis patients, from 0% to 100% with a median of 21.1% among thalassaemia patients, from 1.5% to 54.9% with a median of 16% among multitransfused patients and from 13.1% to 43.4% with a median of 40.3% among patients with coagulation disorders.

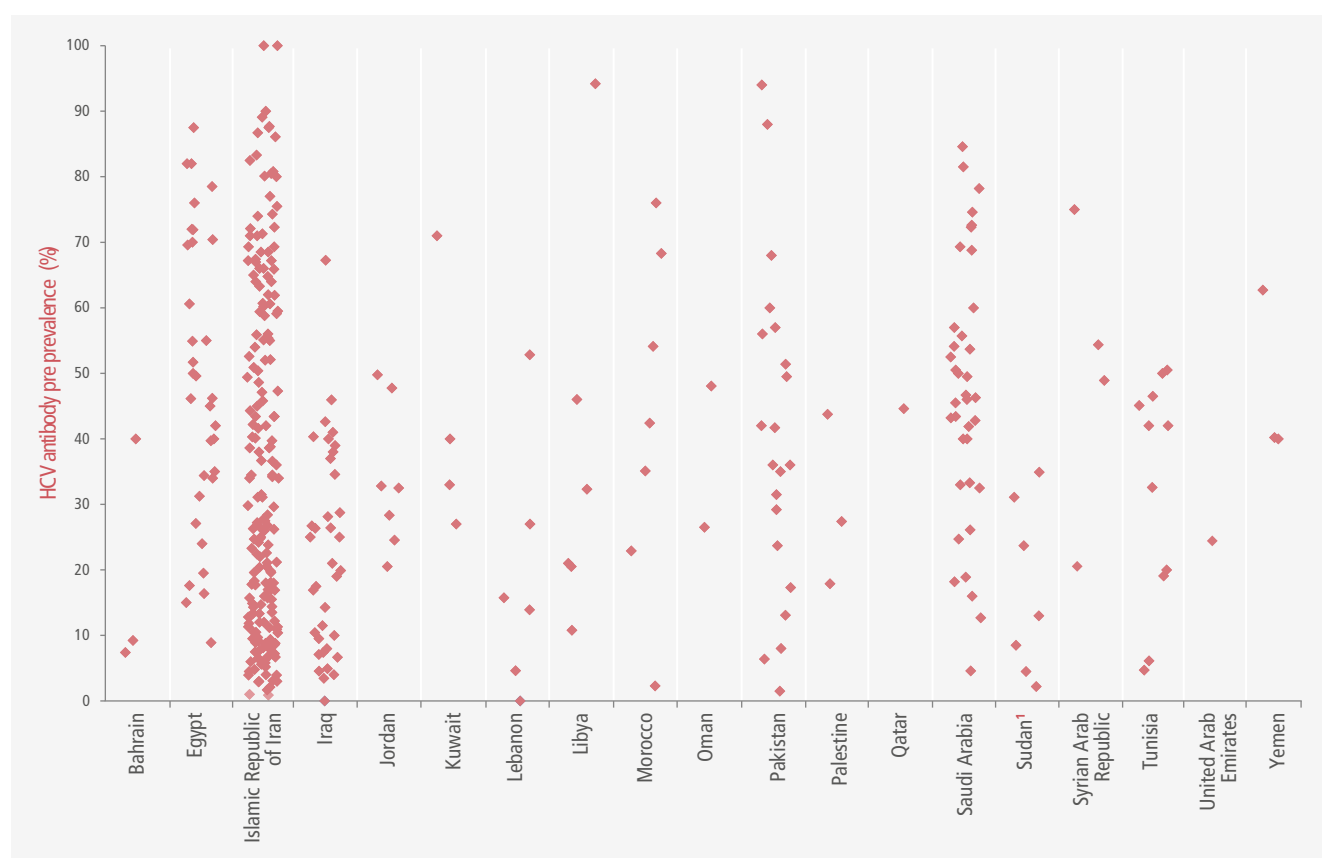


Fig 1. HCV-Ab prevalence among populations with high risk health care exposure to HCV in countries of the Region

1. Available data for Sudan before 2011, the year of independence of South Sudan, may have come from both Sudan and the newly independent Republic of South Sudan.



These findings confirm ongoing transmission of HCV infection in health care settings due to less than optimal infection control procedures. Infectious disease transmission in health care settings continues to be a public health challenge in the Region. Several nosocomial outbreaks, that is infection transmission outbreaks in medical settings, have been documented in the Region

such as in haemodialysis centres (12,13) and hospitals (14–16). There is also evidence of gaps in the implementation of standard precautionary measures in medical settings including private clinics and haemodialysis and blood transfusion units across the Region (17–20).

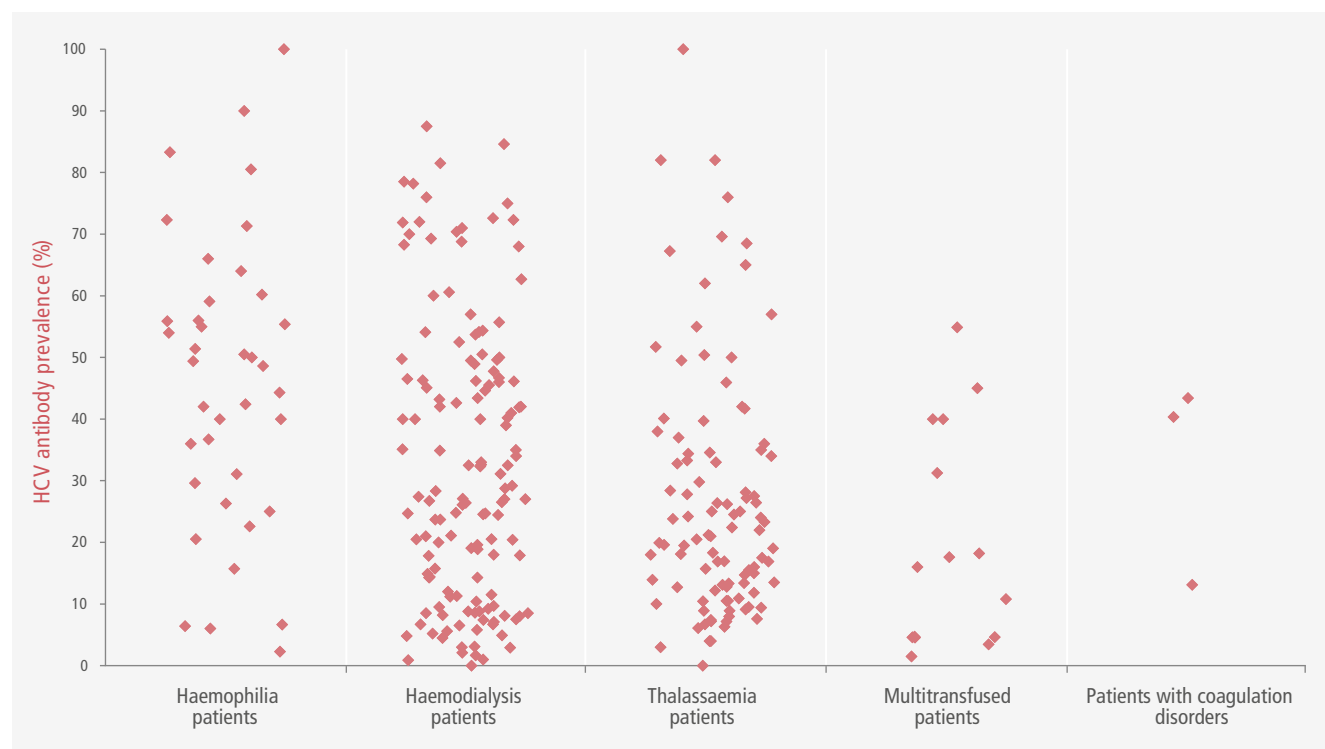


Fig 2. HCV-Ab prevalence among populations with high risk health care exposure to HCV in countries of the Region



Estimates of mean HCV-Ab prevalence among populations with high risk health care exposure to HCV

Table 2 and Fig. 3 show estimates of the mean HCV-Ab prevalence among populations with high risk health care exposure to HCV in each country for which data were available as calculated by pooling all available HCV-Ab prevalence measures through meta-analyses. The estimated mean HCV-Ab prevalence among these populations was high across countries and ranged from 12.0% in Lebanon (95% CI: 4–23%) to 55.4% in Egypt (95% CI: 49.1–61.7%) (Table 2 and Fig. 3).

Table 2. Estimates of HCV-Ab prevalence among populations with high risk health care exposure to HCV in countries of the Region

| Country | Number of studies | Total sample size | HCV-Ab prevalence | | | |
|--------------------------|-------------------|-------------------|-------------------|------------|-----------------------|--|
| | | | Range (%) | Median (%) | Mean ¹ (%) | 95% confidence interval ¹ (%) |
| Bahrain | 4 | 472 | 7.4–40.8 | 8.3 | 14.6 | 2.5–33.9 |
| Egypt | 56 | 7 359 | 8.8–100 | 59.4 | 55.4 | 49.1–61.7 |
| Islamic Republic of Iran | 148 | 36 085 | 0–100 | 19.2 | 26.5 | 21.9–31.4 |
| Iraq | 58 | 6 707 | 0–67.3 | 17.8 | 19.5 | 14.9–24.5 |
| Jordan | 12 | 2 888 | 21.0–59.5 | 34 | 37.0 | 29.3–45.0 |
| Kuwait | 4 | 529 | 27.0–71.3 | 36.5 | 42.6 | 26.1–60.0 |
| Lebanon | 8 | 1 163 | 0–28.6 | 14.5 | 12.0 | 4.0–23.0 |
| Libya | 8 | 3 480 | 0–46.0 | 26.5 | 23.4 | 10.5–39.4 |
| Morocco | 7 | 1 107 | 2.3–75.8 | 42.4 | 43.6 | 18.3–70.9 |
| Oman | 1 | 102 | 26.5 | 26.5 | 26.5 | 18.2–36.1 |
| Pakistan | 19 | 2 489 | 1.5–68.0 | 35.9 | 33.7 | 22.9–45.4 |
| Palestine | 3 | 392 | 6.8–41.4 | 17.9 | 20.5 | 6.4–39.6 |
| Qatar | 1 | 130 | 44.6 | 44.6 | 44.6 | 35.9–53.6 |
| Saudi Arabia | 47 | 43 196 | 0–74.6 | 46.0 | 43.0 | 38.7–47.4 |
| Sudan ² | 6 | 979 | 4.5–34.8 | 18.4 | 17.3 | 8.6–28.2 |
| Syrian Arab Republic | 6 | 1 184 | 21.0–75.0 | 53.8 | 49.8 | 32.6–67.1 |
| Tunisia | 16 | 6 265 | 4.7–50.5 | 26.2 | 26.3 | 20.6–32.4 |
| United Arab Emirates | 1 | 262 | 24.4 | 24.4 | 24.4 | 19.3–30.1 |
| Yemen | 3 | 300 | 40.0–62.7 | 40.2 | 47.4 | 32.7–62.3 |

1. Estimates were generated by summarizing the collective evidence for HCV-Ab prevalence levels using meta-analyses applied to each country of the Region.

2. Available data for Sudan before 2011, the year of independence of South Sudan, may have come from both Sudan and the newly independent Republic of South Sudan.

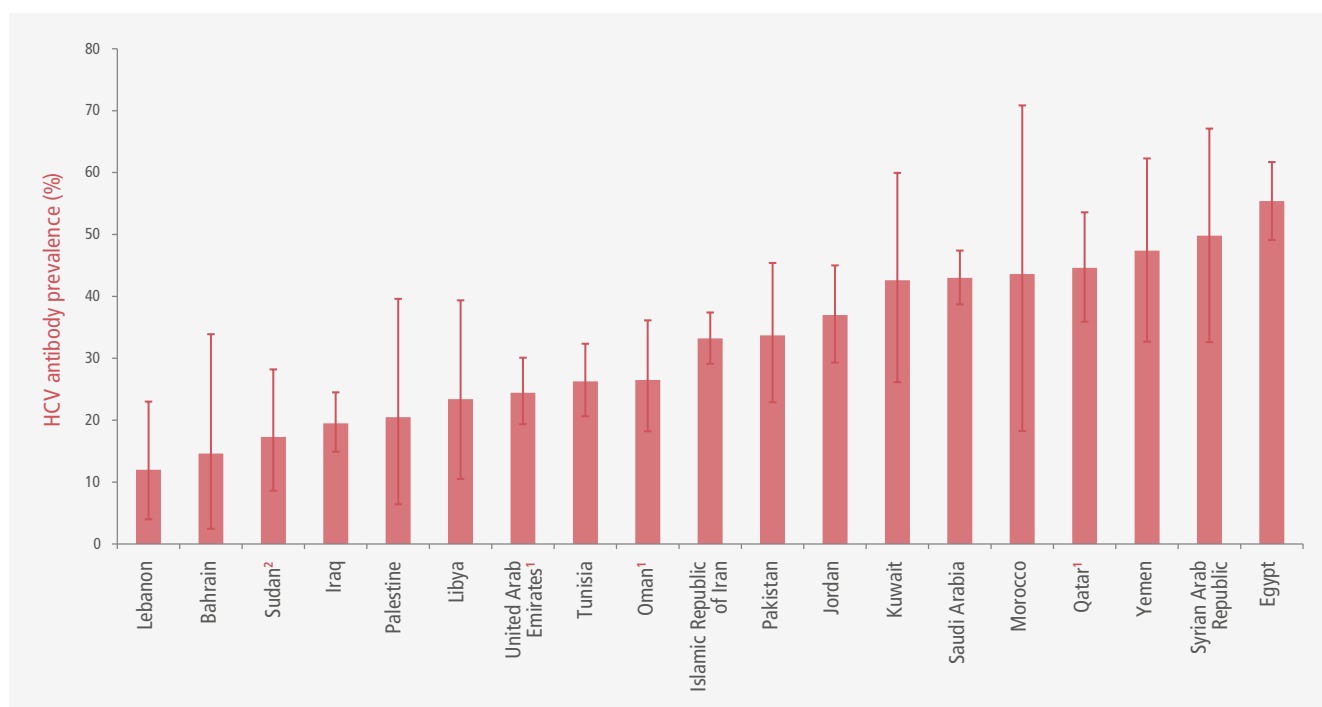


Fig 3. Estimates of the mean HCV-Ab prevalence with the corresponding 95% confidence interval among populations with high risk health care exposure to HCV in countries of the Region

1. HCV-Ab prevalence based on a single study.

2. Available data for Sudan before 2011, the year of independence of South Sudan, may have come from both Sudan and the newly independent Republic of South Sudan.

HCV-Ab prevalence among populations with liver-related conditions

A wide range of HCV-Ab prevalence was observed among populations with liver-related conditions across the Region (Fig. 4). The median HCV-Ab prevalence among these populations was estimated at 33.4% across countries, with the prevalence ranging from 0% to 100%.

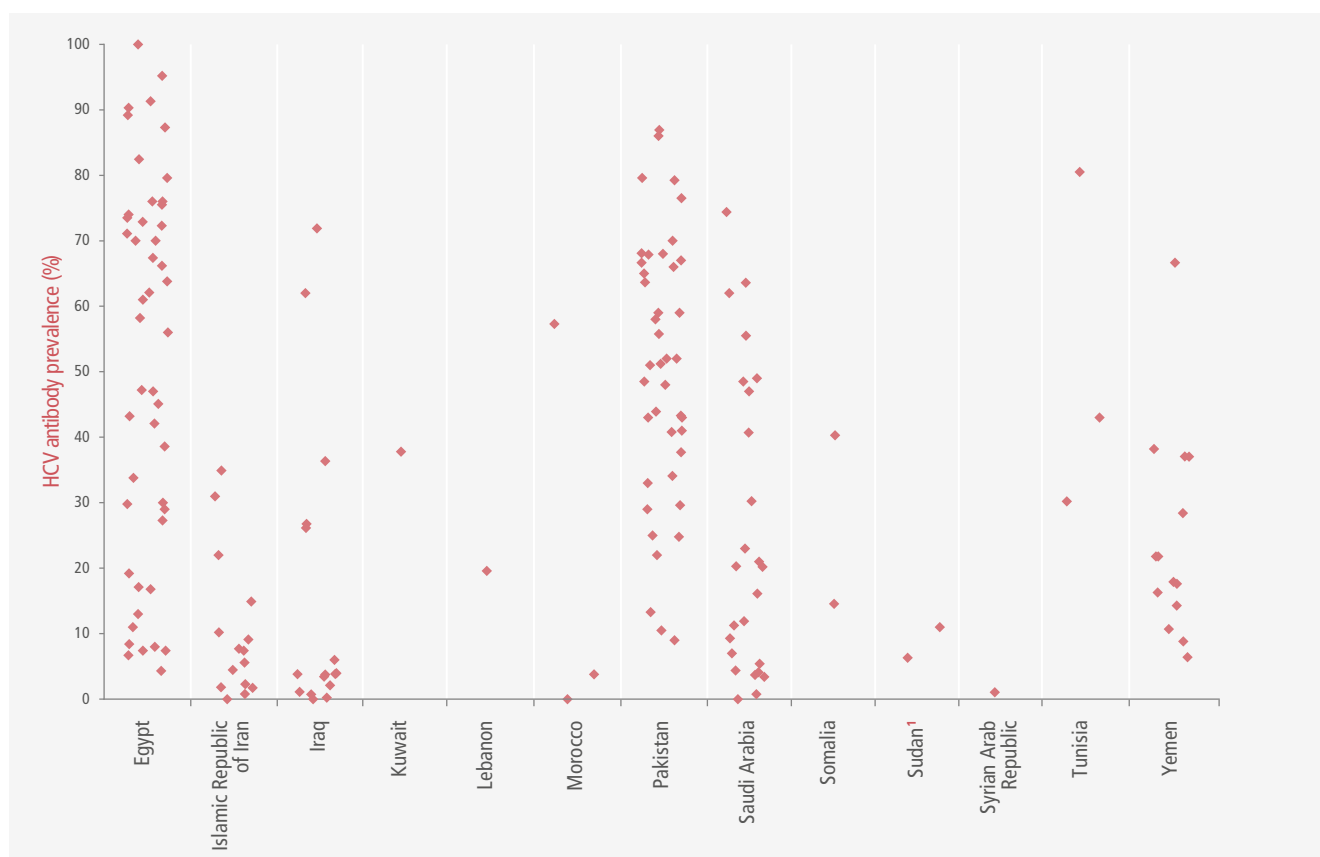


Fig 4. HCV-Ab prevalence among populations with liver-related conditions in countries of the Region

1. Available data for Sudan before 2011, the year of independence of South Sudan, may have come from both Sudan and the newly independent Republic of South Sudan.

HCV-Ab prevalence was high across the various groups of patients with liver-related conditions (Fig. 5). HCV-Ab prevalence ranged from 3.8% to 100% with a median of 47.2% among chronic liver disease patients, from 0% to 55.7% with a median of 26.5% among hepatitis patients, from 0% to 95.2% with a median of 52.0% among hepatocellular carcinoma patients, from 1.7% to 79.6% with a median of 41.0% among patients with liver cirrhosis, from 0.8% to 47.0% with a median of 16.9% among patients

with non-Hodgkin lymphoma, from 0.7% to 82.5% with a median of 24.8% among patients with suspected acute viral hepatitis, and from 0% to 74.4% with a median of 6.9% among acute viral hepatitis patients. These prevalence measures indicate substantial exposure to HCV infection among populations with liver-related conditions in countries of the Region suggesting that HCV infection is a likely cause of these conditions.

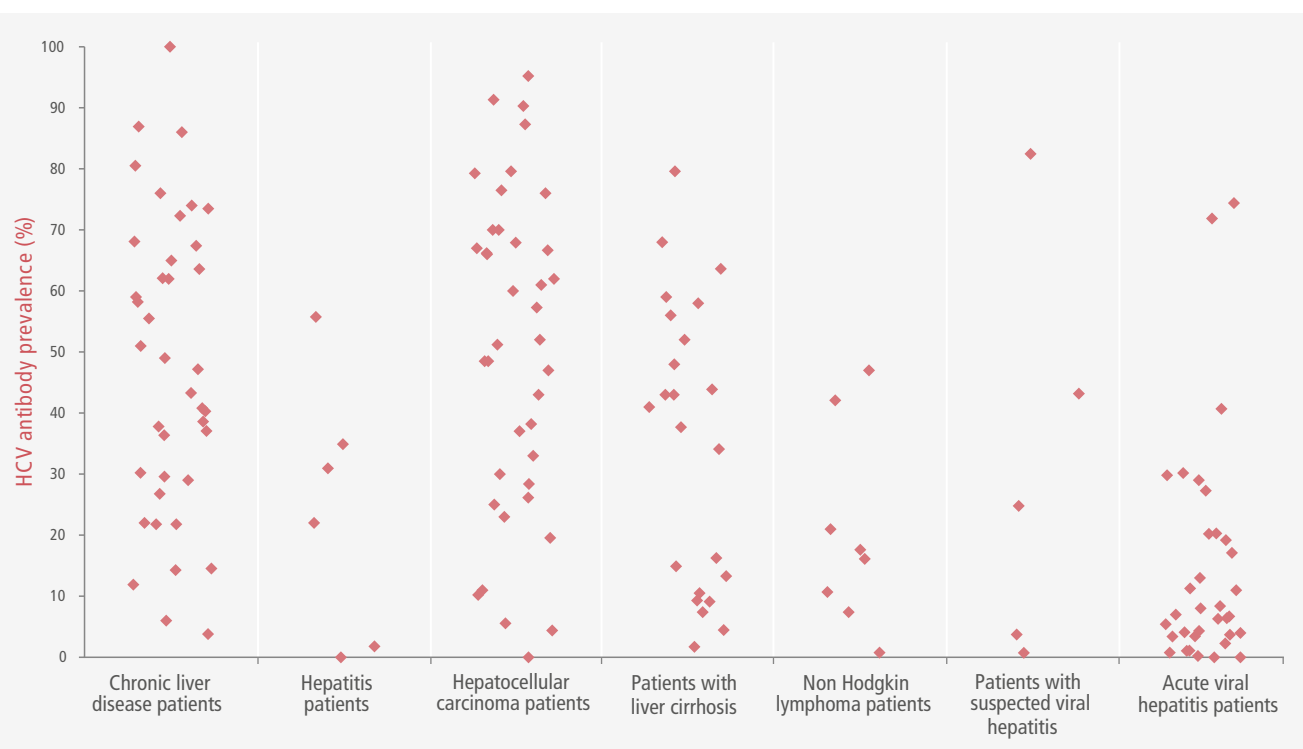


Fig 5. HCV-Ab prevalence among the various populations with liver-related conditions in the Region

Estimates of mean HCV-Ab prevalence among populations with liver-related conditions

Table 3 and Fig. 6 show the estimates of the mean HCV-Ab prevalence among populations with liver-related conditions in countries for which data were available. Mean HCV-Ab prevalence varied across countries from as low as 1.0% in the Syrian Arab Republic (95% CI: 0.1–3.7%) to as high as 56.1% in Egypt (95% CI: 50.5–61.6%). These results indicate that a substantial proportion of the liver disease burden in the Region is likely caused by HCV infection. This is especially so for countries such as Egypt and Pakistan where the prevalence of the infection in the whole population is high compared to other countries (Section 6).

**Table 3.** Estimates of HCV-Ab prevalence among populations with liver-related conditions in countries of the Region

| Country | Number of studies | Total sample size | HCV-Ab prevalence | | | |
|--------------------------|-------------------|-------------------|-------------------|------------|-----------------------|--|
| | | | Range (%) | Median (%) | Mean ¹ (%) | 95% confidence interval ¹ (%) |
| Egypt | 73 | 47 272 | 4.3–100 | 63.8 | 56.1 | 50.5–61.6 |
| Islamic Republic of Iran | 21 | 4 862 | 0–34.9 | 4.8 | 6.1 | 3.6–11.2 |
| Iraq | 31 | 17 460 | 0–76.2 | 3.3 | 6.4 | 4.2–9.0 |
| Kuwait | 1 | 111 | 37.8 | 37.8 | 37.8 | 28.8–47.5 |
| Lebanon ² | 2 | 127 | 0–19.6 | 9.8 | 14.2 | 8.6–21.5 |
| Morocco | 4 | 7 355 | 0–57.3 | 3.07 | 9.3 | 0.0–31.5 |
| Pakistan | 42 | 14 089 | 9.0–86.9 | 51.1 | 49.6 | 44.5–54.8 |
| Qatar | 3 | 977 | 2.7–93.6 | 3.7 | 28.8 | 25.9–31.7 |
| Saudi Arabia | 20 | 11 326 | 1.7–63.6 | 24.6 | 27.3 | 14.7–42.1 |
| Somalia ² | 2 | 172 | 14.6–40.3 | 27.4 | 26.1 | 5.7–54.3 |
| Sudan ^{2,3} | 2 | 131 | 6.3–11.3 | 8.8 | 9.9 | 5.0–16.0 |
| Syrian Arab Republic | 1 | 193 | 1.0 | 1.0 | 1.0 | 0.1–3.7 |
| Tunisia | 7 | 535 | 8.0–80.5 | 42.9 | 39.3 | 22.1–57.8 |
| United Arab Emirates | 1 | 142 | 43.7 | 4.7 | 43.7 | 35.4–52.2 |
| Yemen | 10 | 1 872 | 6.4–38.3 | 19.9 | 21.3 | 12.7–31.3 |

1. Estimates were generated by summarizing the collective evidence for HCV-Ab prevalence levels using meta-analyses applied to each country of the Region.

2. For countries where only two studies were available, HCV-Ab prevalence was estimated using the average of prevalence measures reported in these studies.

3. Available data for Sudan before 2011, the year of independence of South Sudan, may have come from both Sudan and the newly independent Republic of South Sudan.

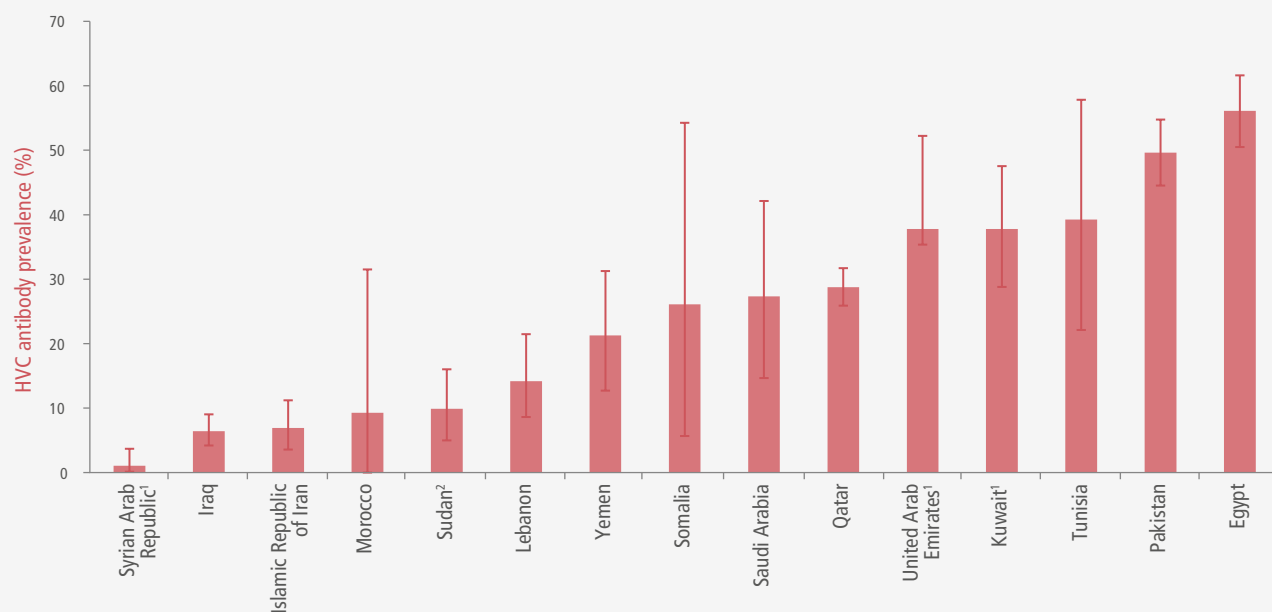


Fig 6. Estimates of the mean HCV-Ab prevalence with the corresponding 95% confidence interval among populations with liver-related conditions in countries of the Region

1. HCV-Ab prevalence based on a single study.

2. Available data for Sudan before 2011, the year of independence of South Sudan, may have come from both Sudan and the newly independent Republic of South Sudan.

Key highlights

- The incidence of HCV infection among populations with high risk health care exposure to HCV in the Region is substantial.
- There is evidence of ongoing HCV transmission due to less than optimal infection control procedures in specific health care settings in at least some countries.
- HCV-Ab prevalence among populations with high risk health care exposure to HCV is high with about half of the studies reporting levels exceeding 28% among populations such as haemodialysis, thalassaemia and haemophilia patients.
- High HCV-Ab prevalence levels are reported among populations with liver-related conditions suggesting that HCV infection is a major cause of liver disease burden in the Region.

4

HCV epidemiology among people who inject drugs

21 ▪ PWID population size estimation

22 ▪ Injecting risk behaviour and exposure to HCV
▪ HCV-Ab prevalence among PWID

23 ▪ Estimates of mean HCV-Ab prevalence among PWID

25 ▪ Key highlights

56 ▪ References





4.

HCV epidemiology among people who inject drugs

20

HCV epidemiology among people who inject drugs



Section 4 presents an overview of the epidemiological evidence for HCV infection among PWID across countries. This section describes the size of the PWID population in each country, discusses PWID's injecting risk environment, reviews epidemiological evidence for HCV infection among PWID across the Region and provides estimates of HCV-Ab prevalence among this population in each country.





PWID population size estimation

It is estimated that there are about 590 000 PWID in the Region, based on a systematic review of PWID (1) and updated with recent data (2–11). The Islamic Republic of Iran, Pakistan and Egypt have the largest numbers with 185 000, 117 600 and 90 800 PWID, respectively (1) (Table 4). The weighted population proportion of injecting drug use in the Region is 0.15 per 100 adults (1). The population proportion is lowest in Somalia at 0.02% and highest in the Islamic Republic of Iran at 0.33% (Table 4). Injecting drug use in the Region appears to be highly concentrated among men, with few data on female PWID who remain a vulnerable and highly hidden population (1).

Table 4. Estimates of the median number and population proportion of PWID in countries of the Region

| Country | Number of PWID | Population proportion of PWID (%) |
|--------------------------|------------------|-----------------------------------|
| Afghanistan | 18 820 | 0.11 |
| Bahrain | 1 937 | 0.18 |
| Djibouti | 831 ¹ | 0.15 |
| Egypt | 90 809 | 0.16 |
| Islamic Republic of Iran | 185 000 | 0.33 |
| Iraq | 34 673 | 0.17 |
| Jordan | 4 850 | 0.11 |
| Kuwait | 4 050 | 0.14 |
| Lebanon | 3 207 | 0.08 |
| Libya | 4 446 | 0.11 |
| Morocco | 18 000 | 0.08 |
| Oman | 4 250 | 0.12 |
| Pakistan | 117 632 | 0.10 |
| Palestine | 1 850 | 0.07 |
| Qatar | 1 190 | 0.06 |
| Saudi Arabia | 16 800 | 0.08 |
| Somalia | 1 000 | 0.02 |
| Sudan | 37 828 | 0.17 |
| Syrian Arab Republic | 8 000 | 0.07 |
| Tunisia | 11 000 | 0.14 |
| United Arab Emirates | 4 800 | 0.06 |
| Yemen | 19 770 | 0.13 |

1. As there were no data for Djibouti, the number of PWID was estimated using the regional average for the population proportion of PWID and the size of the adult population in Djibouti.



Injecting risk behaviour and exposure to HCV

Evidence on PWID in the countries shows generally a high injecting risk environment (1, 12). The key risk behaviour that exposes PWID to HCV infection is the use of non-sterile injecting equipment. Several studies have documented relatively high levels of sharing of needles or syringes, whether it is sharing during the last injection, past month, past six months, past year or during lifetime (1). Available data indicate that the percentage of PWID who engaged in sharing of needles or syringes at least once in their lifetime was as high as 71% in Jordan (13), 79% in Pakistan (14), 85% in Libya (15), 95% in the Islamic Republic of Iran (16), and 97% in Oman (17). The median prevalence in the Region for sharing needles or syringes during the last injection was 23% (1).

PWID in the Region inject drugs at a median of 2.2 injections per day (1). Higher levels of 3.3 (18) and 5.7 (19) injections per day have been reported among some PWID in the Islamic Republic of Iran and Afghanistan, respectively. The median age at first injection is 26 years and the duration of injecting drugs is estimated to be close to 10 years (1).

The social and injecting networks of PWID play an important role in determining the risk of HCV acquisition. The countries appear to have different types of risk networks both across countries and sometimes within any one country (12, 20). In Lebanon and the Syrian Arab Republic, for example, it appears that PWID form small closed networks with injecting occurring in private homes and among friends, and not in large groups or at shooting galleries (21, 22). On the other hand, in the Islamic Republic of Iran and Pakistan injecting networks often seem to be well connected and there are reports of injecting and sharing occurring among people who are not necessarily socially related, for example in shooting galleries where PWID can rent or borrow needles and syringes (20, 23). In Pakistan, most injecting appears to occur

in groups and in public places, and the reported use of “street doctors” or professional injectors is common as well as a high frequency of reuse of injecting equipment (1, 24).

HCV-Ab prevalence among PWID

There have been many HCV-Ab prevalence studies among PWID in the Region (Fig. 7). The largest numbers of studies were from the Islamic Republic of Iran, Pakistan and Afghanistan. In a few countries, namely Lebanon, Libya, Morocco, Palestine and Tunisia, there were only one or two studies reporting HCV-Ab prevalence measures among PWID, but they were of high quality and included integrated bio-behavioural surveillance and rigorous sampling methodologies (1).

There were variations in HCV-Ab prevalence levels across and within countries (Fig. 7). HCV-Ab prevalence levels were generally in the intermediate to high range compared to those reported globally (25). Very high HCV-Ab prevalence among PWID was reported in some countries, such as Afghanistan at 70% in Herat (26), Egypt at 63% in Alexandria (27), Islamic Republic of Iran at over 80% among PWID prisoners in Tehran (28–30), Libya at 94% in Tripoli (15), Pakistan at 94% in Karachi (31) and Saudi Arabia at 75% in Jeddah (32). These figures suggest that sharing of injecting equipment is a common practice among PWID in countries.

It is worth noting that these studies capture HCV infection only among current PWID; however, they represent only part of the population that acquired HCV infection through injecting drug use. It is likely that a significant proportion of currently infected individuals in the general population in some of the countries could be former PWID (as opposed to current PWID). For example, while 0.3% of the population are current PWID in the United States, 2.6% of the population reported ever injecting drugs (lifetime PWID), and about half of both current and former PWID were infected with HCV (33).

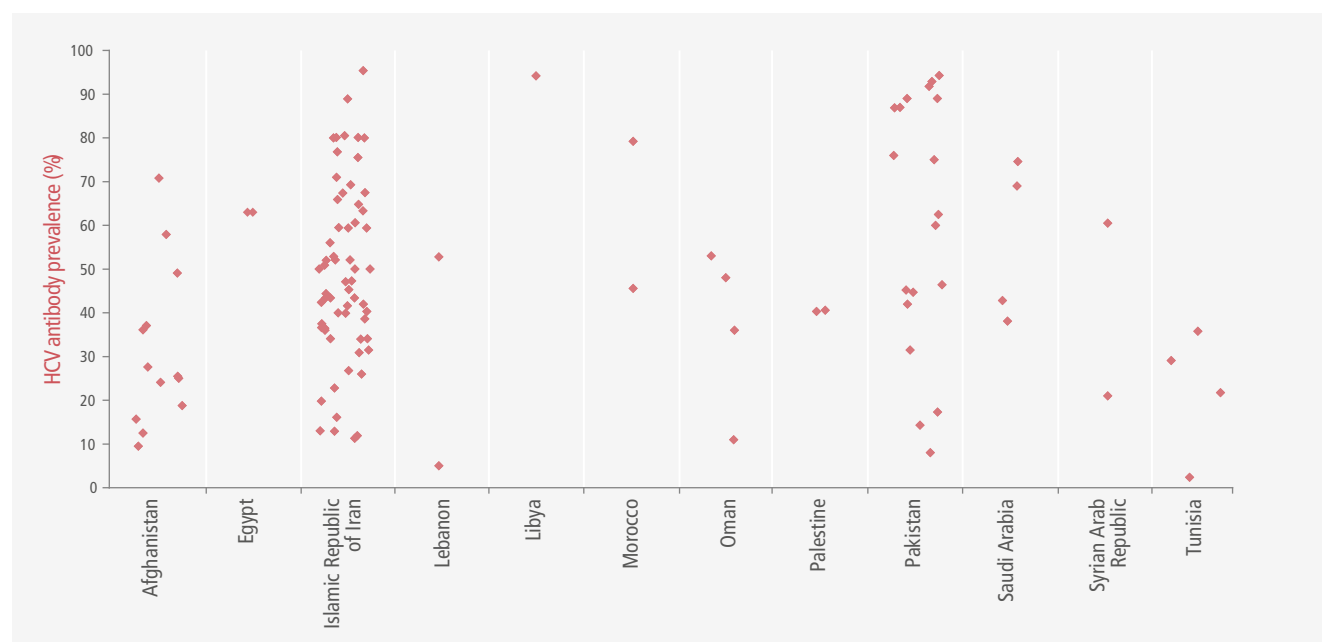


Fig 7. HCV-Ab prevalence among people who inject drugs in countries of the Region

Estimates of mean HCV-Ab prevalence among PWID

Table 5 and Fig. 8 show the estimates of the mean HCV-Ab prevalence among PWID generated through meta-analyses of HCV data for each country for which data were available. The highest HCV-Ab prevalence among PWID was estimated in Libya at 94.2% (95% CI: 91.1–96.5%) in the first round of surveillance in 2010, however, this was from only one available study for this country (15). In this same study, HIV prevalence was found to be 87%, one of the highest prevalence levels of HIV reported among PWID globally (15). Restrictions imposed on the sale of needles

and syringes at pharmacies in the late 1990s in Libya may have contributed to an increase in the use of non-sterile injecting equipment and seems to have consequently led to a rapid increase in HCV and HIV infections among PWID (34, 35).

Apart from Libya, the mean HCV-Ab prevalence among countries is estimated at just over 60% in Egypt, Morocco and Pakistan, in the range of 50% to 60% in the Islamic Republic of Iran, Oman and Saudi Arabia, between 30% and 40% in Afghanistan, Palestine and the Syrian Arab Republic, and below 30% in Lebanon and Tunisia (Table 5, Fig. 8). The median HCV-Ab prevalence among PWID across all countries is 45%, comparable to global levels (36).

**Table 5.** Estimates of HCV-Ab prevalence among people who inject drugs in countries of the Region

| Country | Number of studies | Total sample size | Range (%) | Median (%) | Mean (%) ¹ | 95% confidence interval ¹ (%) |
|-----------------------------------|-------------------|-------------------|-----------|------------|-----------------------|--|
| Afghanistan | 13 | 7 680 | 9.5–70.8 | 25.5 | 31.7 | 22.6–41.6 |
| Egypt | 1 | 100 | | 63.0 | 63.0 | 52.8–72.4 |
| Islamic Republic of Iran | 58 | 18 931 | 11.3–88.9 | 46.2 | 49.9 | 45.2–54.5 |
| Lebanon ² | 2 | 146 | 5.0–52.8 | 28.9 | 28.9 | 21.5–36.3 |
| Libya | 1 | 328 | | 94.2 | 94.2 | 91.1–96.5 |
| Morocco ² | 2 | 535 | 45.6–79.2 | 62.4 | 62.4 | 58.3–66.5 |
| Oman ² | 2 | 572 | 53.0–48.1 | 50.5 | 50.5 | 46.4–54.6 |
| Pakistan | 17 | 3 658 | 8.0–94.3 | 60.0 | 61.8 | 45.5–76.8 |
| Palestine ² | 2 | 480 | 40.3–40.6 | 40.5 | 40.5 | 36.1–44.8 |
| Saudi Arabia | 4 | 3 001 | 38.1–74.6 | 55.9 | 56.6 | 38.3–74.0 |
| Syrian Arab Republic ² | 2 | 95 | 21.0–60.5 | 40.8 | 40.8 | 30.9–50.7 |
| Tunisia | 3 | 1 508 | 2.4–35.8 | 29.1 | 21.1 | 7.8–38.7 |

1. Estimates generated by summarizing the collective evidence for HCV-Ab prevalence levels using meta-analyses applied to each country of the Region.

2. For countries where only two studies were available, HCV-Ab prevalence was estimated using the average of prevalence measures reported in these studies.



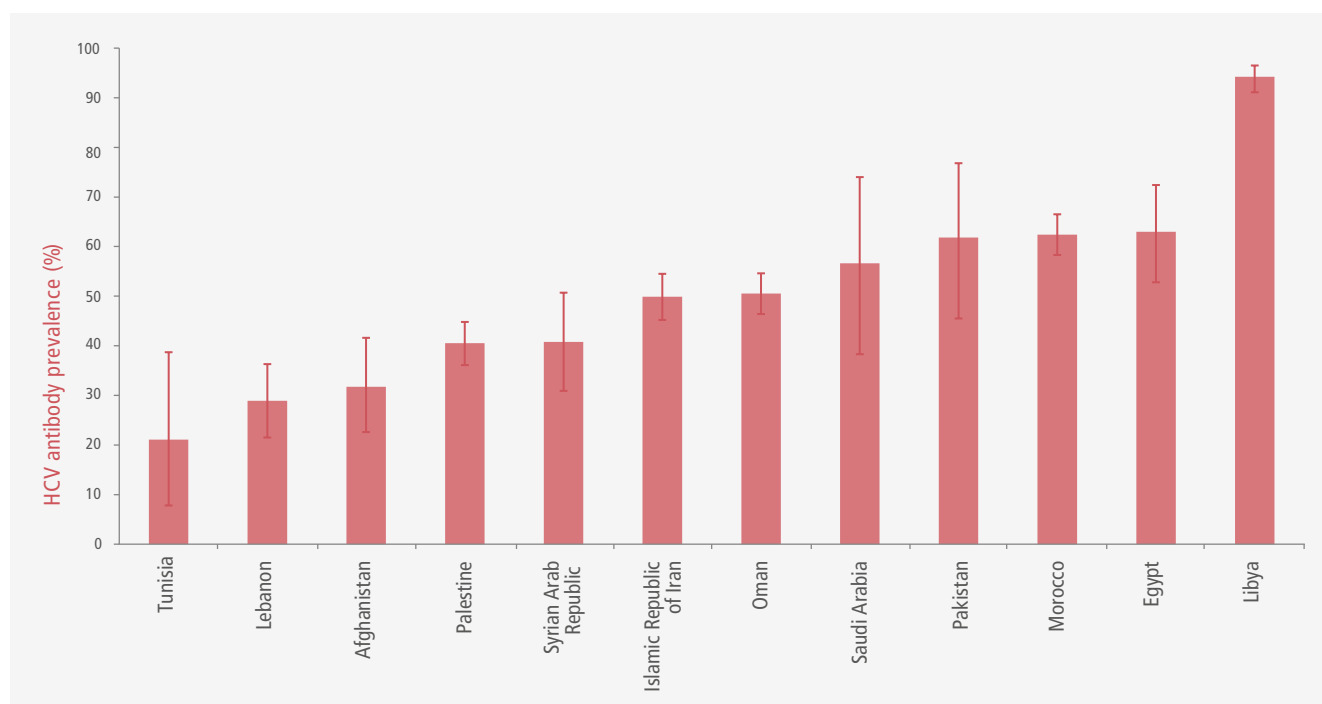


Fig 8. Estimates of the mean HCV-Ab prevalence with the corresponding 95% confidence interval among PWID in countries of the Region

Key highlights

- There are over half a million PWID across countries.
- Nearly half of PWID in the Region are infected with HCV.
- Very high HCV-Ab prevalence figures exceeding 60% have been reported among PWID in several countries.
- PWID in the Region engage in high levels of injecting risk behaviour, specifically sharing of unsterile needles and syringes, which exposes them to HCV infection.

5

HCV epidemiology among populations at intermediate risk of exposure to HCV

28

- HCV incidence among intermediate risk populations
- HCV-Ab prevalence among intermediate risk populations

30

- Estimates of mean HCV-Ab prevalence among intermediate risk populations

32

- Key highlights

59

- References





5.

HCV epidemiology among populations at intermediate risk of exposure to HCV



This section overviews the epidemiological evidence for HCV infection among populations at intermediate risk of acquiring HCV infection, i.e. populations with a risk of infection that is higher than the general population but lower than the populations with high risk health care exposure to HCV and PWID.

The prevalence of HCV infection among this population is also estimated for each country. Examples of people included in the intermediate risk populations are health care workers, household contacts of HCV-infected patients, hospitalized populations, patients with diabetes,³ men who have sex with men, prisoners and barbers, among others. This mix of populations includes populations who could have been exposed to HCV due to behavioural factors as well as other populations, such as those with diabetes, among whom the link with HCV is more complex. People with diabetes could be at increased risk of exposure to HCV because of medical care, but evidence also suggests that development of diabetes could be a consequence of HCV infection (1,2).

3. Patients with diabetes are included among intermediate risk populations given their potential exposure to insulin injections or to sharing of medical testing kits such as glucometers.



HCV-Ab incidence among intermediate risk populations

Only Egypt has reported studies assessing HCV-Ab incidence among intermediate risk populations (Table 6). Three studies were conducted among health care workers (3–5), one of which reported no incidence of HCV infection (4). The HCV incidence rate in the other two studies was measured at 2.0 (3) and 7.3 (5) per 1 000 person-years, suggesting a substantial risk for medical personnel to acquire HCV through contact with contaminated equipment or blood products in health care facilities. A fourth study showed an increased risk of HCV infection among children who were born HCV-negative but whose mothers were HCV-infected (6).

Table 6. Studies reporting HCV-Ab incidence among intermediate risk populations in Egypt, the only country in the Region reporting this measure

| First author, year of publication [citation] | Year(s) of data collection | Population | Sample size | HCV seroconversion risk (relative to total sample size) ¹ | Incidence rate (per 1 000 person – years) ² | Duration of follow-up (months) |
|--|----------------------------|----------------------------------|-------------|--|--|--------------------------------|
| Egypt | | | | | | |
| Abdelwahab, 2013 (3) | 2008–2011 | Health care workers | 651 | 0.3 | 2.0 | 17.0 |
| Munier, 2013 (4) | 2008–2010 | Health care workers | 73 | 0.0 | | 24.0 |
| Okasha, 2015 (5) | 2008 | Health care workers | 402 | | 7.3 | 18.0 |
| Saleh, 2010 (6) | 2000–2006 | Children of HCV-infected mothers | 2 852 | 0.5 | 2.7 | 60.0 |

1. Proportion of people who acquired the infection during the follow-up duration of the study.

2. Number of people who acquired the infection over the total duration of follow-up for all subjects included in the study.

HCV-Ab prevalence among intermediate risk populations

There were close to 300 studies reporting HCV-Ab prevalence among populations at intermediate risk of exposure to HCV infection in the countries (Fig. 9). While a large number of studies was available for some countries, such as the Islamic Republic of Iran, Egypt and Pakistan, there were no data on intermediate risk populations in other countries like Bahrain, Djibouti and Qatar.

A wide range of HCV-Ab prevalence levels was reported among populations at intermediate risk of exposure to HCV infection across the countries for which data

were available (Fig. 9). In Egypt, HCV-Ab prevalence among this population ranged from 0% to 90% with a median of 12.8% – the highest across all countries. High infection levels were also found in Pakistan where HCV-Ab prevalence ranged from 1.3% to 37.9% with a median of 12.4%. HCV-Ab prevalence also varied from 2.0% to 54.1% in Libya with a median of 7.1%, and from 1% to 39.7% in Tunisia with a median of 10.8%. For the rest of the countries, HCV-Ab prevalence among intermediate risk populations was mostly less than 10%, with a median of 3.5%. Clearly these infection levels are lower than those observed among populations with high risk health care exposure and PWID (Sections 3 and 4), but higher than that observed among the general population (Section 6).

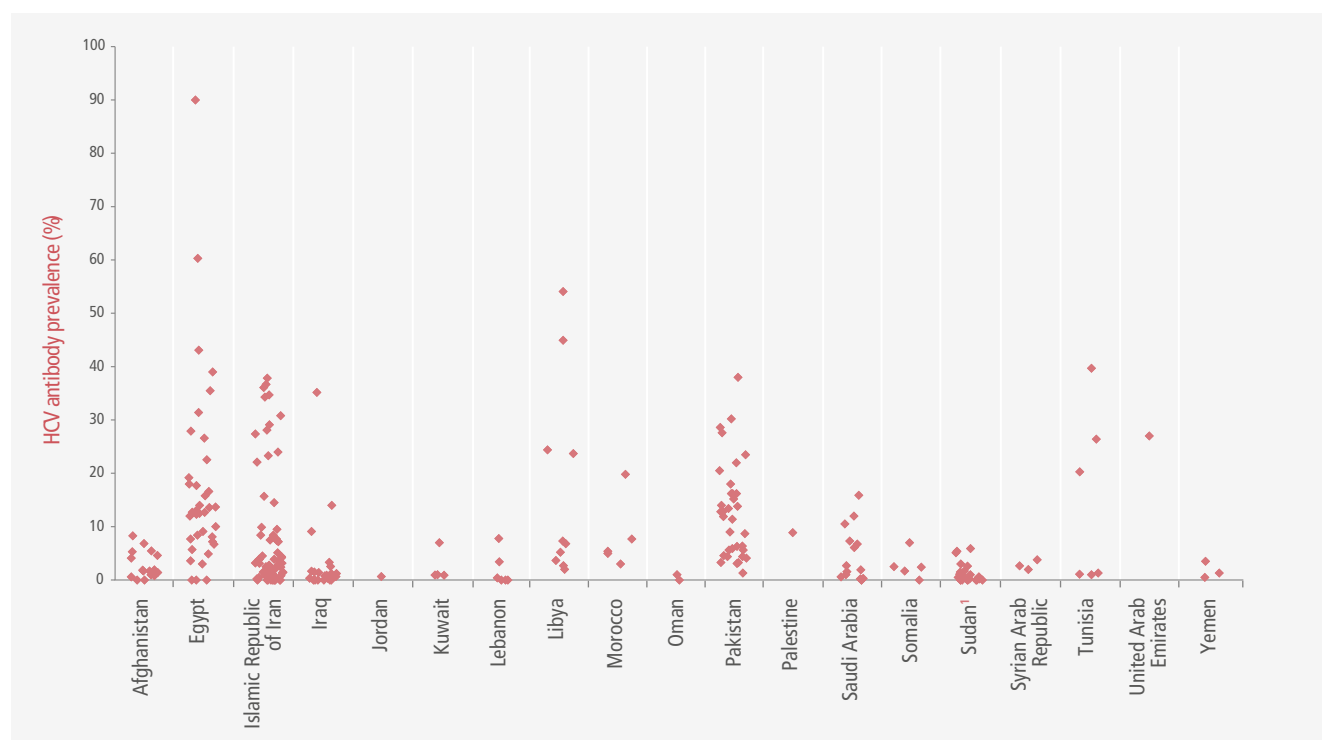


Fig 9. HCV-Ab prevalence among the intermediate risk populations in countries of the Region

1. Available data for Sudan before 2011, the year of independence of South Sudan, may have come from both Sudan and the newly independent Republic of South Sudan.

Fig. 10 shows HCV-Ab prevalence among various intermediate risk populations across the countries. The prevalence among inpatient populations ranged from 0% to 90% with a median across countries of 6.9%. Among outpatients, HCV-Ab prevalence ranged from 0% to 22.5% with a median of 1%. Among health care workers, HCV-Ab prevalence ranged from 0% to 16.6% with a median of 1%. These prevalence levels suggest an elevated risk of infection among these population in comparison to the general population (Section 6).

Studies conducted among people with diabetes reported a wide range of HCV-Ab prevalence from 0.2% to 60.3% with a median of 15.0%. High infection levels reaching up to 38% were observed among household contacts of HCV-infected patients with a median of 10.9%. HCV-Ab prevalence among barbers and their clients varied from 0% in the Islamic Republic of Iran to 12.7% in Egypt with a median of 5% across all countries.

As for prisoners, HCV-Ab prevalence ranged from 0% to 37.9% with a median of 4.4%. Incarcerated populations have substantial HCV infection levels, probably because of injecting drug use during or before imprisonment.

Prisoners also commonly engage in risk behaviours that may increase their risk of acquiring bloodborne infections, such as tattooing and unprotected anal sex (7). The latter is an established risk factor for HCV infection among men who have sex with men (8,9) and the HCV-Ab prevalence among this population varied from 0% to 23.5% with a median of 1.0%. Among female sex workers, HCV-Ab prevalence ranged from 0% to 9.9% with a median of 1.1%. Injecting drug use is not uncommon among female sex workers in countries (10). HCV-Ab prevalence levels varying from 0% to 34.3% with a median of 2.4% were also reported among homeless people—a population that is vulnerable to injecting drug use among other risk factors (10). Lastly, substantial HCV-Ab prevalence levels ranging between 1.7% and 39.7% with a median of 13.8% were reported among HIV-positive patients, probably because of a history of injecting drug use.

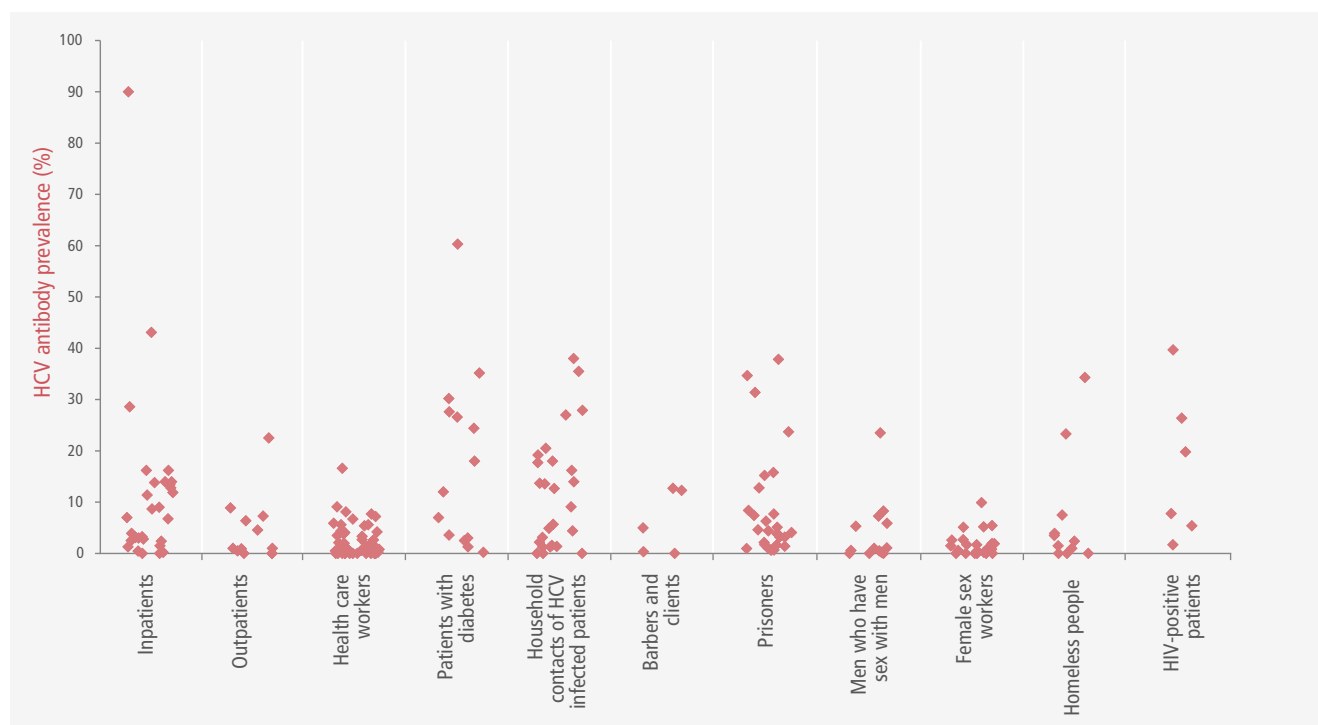


Fig 10. HCV-Ab prevalence among various populations at intermediate risk of exposure to HCV infection in the Region

Estimates of mean HCV-Ab prevalence among intermediate risk populations

Table 7 and Fig. 11 show the estimates of the mean HCV-Ab prevalence among intermediate risk populations generated through meta-analyses of available HCV data for each country for which data were available. A high estimate was found for Egypt with a mean HCV-Ab prevalence of 16.8% (95% CI: 12.5–21.5%). High levels were also found in the United Arab Emirates of 30.5% (95% CI: 14.9–48.6%), possibly because of a large representation of Egyptian workers and/

or possibly because of non-representative samples and small number of studies. Estimated mean HCV-Ab prevalence was high for Libya at 13.4% (95% CI: 5.3–24.4%), Pakistan at 11.6% (95% CI: 8.5–15.1%) and Tunisia at 10.8% (95% CI: 1.8–25.7%). For the rest of the countries, the mean HCV-Ab prevalence among intermediate risk populations was estimated at less than 10% (Table 7 and Fig. 11). It should be noted that for several countries few studies were identified and therefore these estimates may not be representative of the wider intermediate risk populations in these countries.

**Table 7.** Estimates of HCV-Ab prevalence among the intermediate risk populations in countries of the Region

| Country | Number of studies | Total sample size | HCV-Ab prevalence | | | |
|--------------------------|-------------------|-------------------|-------------------|------------|-----------------------|--|
| | | | Range (%) | Median (%) | Mean ¹ (%) | 95% confidence interval ¹ (%) |
| Afghanistan | 16 | 6 356 | 0–8.3 | 1.8 | 2.3 | 1.3–3.7 |
| Egypt | 49 | 10 760 | 0–90.4 | 12.9 | 16.8 | 12.5–21.5 |
| Islamic Republic of Iran | 66 | 33 938 | 0–48.0 | 3.2 | 6.2 | 3.3–9.8 |
| Iraq | 35 | 13 761 | 0–35.2 | 0.8 | 1.2 | 0.6–1.9 |
| Jordan | 1 | 152 | 0.7 | 0.7 | 0.7 | 0.0–3.6 |
| Kuwait | 4 | 2 543 | 0.9–17.7 | 2.1 | 3.9 | 0.5–10.1 |
| Lebanon | 7 | 1 050 | 0–7.8 | 0.7 | 1.2 | 0.1–3.3 |
| Libya | 11 | 27 130 | 2.0–54.1 | 6.8 | 13.4 | 5.3–24.4 |
| Morocco | 6 | 3 640 | 3.0–19.8 | 5.6 | 7.3 | 4.1–11.2 |
| Oman ² | 2 | 247 | 0–1.0 | 0.5 | 0.5 | 0.0–2.2 |
| Pakistan | 36 | 119 171 | 1.3–37.9 | 12.4 | 11.6 | 8.5–15.1 |
| Palestine | 1 | 124 | 8.9 | 8.9 | 8.9 | 4.5–15.3 |
| Saudi Arabia | 20 | 6 392 | 0.0–22.5 | 2.6 | 4.2 | 2.2–6.8 |
| Somalia | 5 | 702 | 0–7.0 | 2.4 | 1.7 | 0.0–4.9 |
| Sudan ³ | 23 | 6 450 | 0–5.9 | 0.5 | 0.7 | 0.2–1.3 |
| Syrian Arab Republic | 4 | 725 | 2.0–5.9 | 3.2 | 3.0 | 1.8–4.5 |
| Tunisia | 6 | 3 371 | 1.0–39.7 | 10.8 | 10.8 | 1.8–25.7 |
| United Arab Emirates | 6 | 631 | 7.7–73.9 | 26.5 | 30.5 | 14.9–48.6 |
| Yemen | 3 | 1 322 | 0.5–3.5 | 1.2 | 1.6 | 0.4–3.6 |

1. Estimates were generated by summarizing the collective evidence for HCV-Ab prevalence levels using meta-analyses applied to each country.

2. For countries where only two studies were available, HCV-Ab prevalence was estimated using the average of prevalence measures reported in these studies.

3. Available data for Sudan before 2011, the year of independence of South Sudan, may have come from both Sudan and the newly independent Republic of South Sudan.

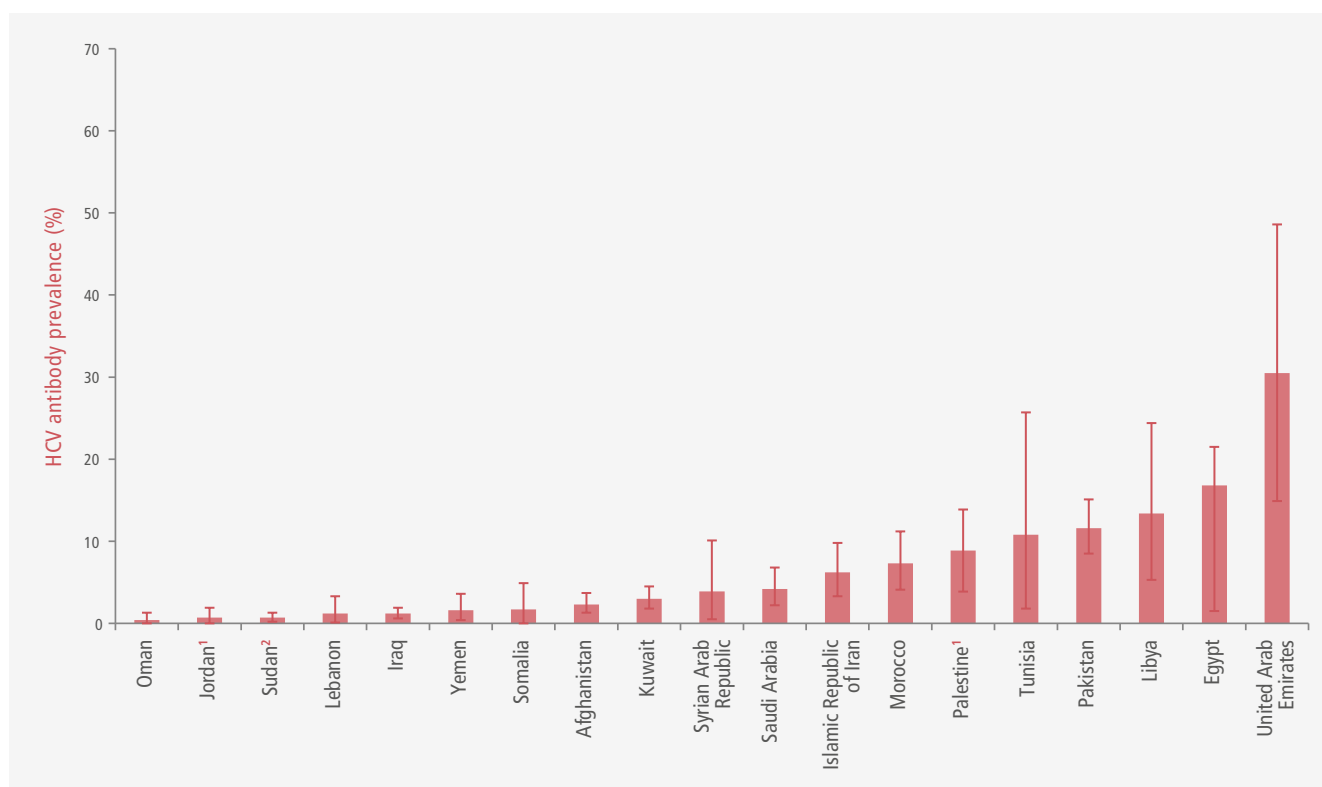


Fig 11. Estimates of the mean HCV-Ab prevalence with the corresponding 95% confidence interval among the intermediate risk populations in countries of the Region

1. HCV-Ab prevalence based on a single study.

2. Available data for Sudan before 2011, the year of independence of South Sudan, may have come from both Sudan and the newly independent Republic of South Sudan.

Key highlights

- HCV-Ab prevalence among populations at intermediate risk of exposure to HCV infection is about 4% in the countries, higher than that observed among the general population but much lower than that observed among populations with high risk health care exposure and PWID.
- The higher HCV-Ab prevalence levels among hospitalized populations and health care workers suggest health care-related exposures in the Region.
- Prisons are a setting where substantial levels of HCV-Ab prevalence are found, probably because of injecting drug use during or before incarceration, and possibly because of other risk behaviours such as tattooing and unprotected anal sex.

6

HCV epidemiology among the general population

34 ▪ Incidence of HCV infection among the general population

35 ▪ HCV-Ab prevalence among the general population

37 ▪ Estimates of mean HCV-Ab prevalence among the general population

39 ▪ Key highlights

59 ▪ References





6.

HCV epidemiology among the general population

34



Section 6 overviews the epidemiological evidence of HCV infection among the general population across countries and provides estimates of HCV-Ab prevalence among the general population in each country.

The general population includes populations that are at low risk of infection such as healthy children, antenatal clinic attendees, pregnant women, blood donors and individuals presenting for pre-employment or pre-marital screening, among others. It is important to note that the meta-analysis estimates provided below include all studies that are available for countries of the Region. However, the scope of available evidence in terms of the number of studies, the type of general populations surveyed and the geographical coverage vary across countries. Accordingly, the estimates for the general population presented here for a specific country may not always be representative of HCV-Ab prevalence in the total population of that country.

HCV-Ab incidence among the general population

There were only a few studies reporting HCV-Ab incidence among the general population across the Region ([Table 8](#)). A total of five studies were identified, four of which were conducted in Egypt and a single study was conducted in Iraq. The incidence rate of HCV infection in Egypt ranged from 0.8 to 6.8 per 1 000 person – years in these studies (1–3), suggesting ongoing HCV transmission at some level in the population (4,5). The only incidence study identified from Iraq was conducted among healthy children and reported no incidence of HCV infection (6).

**Table 8.** Studies reporting HCV-Ab incidence among the general population in the two countries of the Region for which data were available

| First author, year of publication [citation] | Year(s) of data collection | Population | Sample size | HCV seroconversion risk (relative to total sample size) ¹ | Incidence rate (per 1 000 person – years) ² | Duration of follow-up (months) |
|--|----------------------------|--|-------------|--|--|--------------------------------|
| Egypt | | | | | | |
| Mostafa, 2010 (1) | 2001–2006 | Household members surveyed in 3 villages in Menoufia governorate, Nile Delta | 3 184 | | 2.4 | |
| Mohamed, 2005 (2) | 1997–2000 | Household members surveyed in Aghour el Soughra village, Nile Delta | 2 463 | | 6.8 | 19.0 |
| Mohamed, 2005 (2) | 1997–2000 | Household members surveyed in Sallam village, Upper Egypt | 4 275 | | 0.8 | 19.0 |
| Saleh, 2008 (3) | 1997–2006 | Pregnant women surveyed in 3 villages in Menoufia governorate, Nile Delta | 2 171 | | 5.2 | 26.0 |
| Iraq | | | | | | |
| Al-Ani, 2011 (6) | 1997–2006 | Healthy children | 60 | | | 6.0 |

1. Proportion of people who acquired the infection during the follow-up duration of the study.

2. Number of people who acquired the infection over the total duration of follow-up for all subjects included in the study.

HCV-Ab prevalence among the general population

Hundreds of studies have been conducted among general populations in the Region. With a national prevalence exceeding 10% among the adult population, Egypt has the highest HCV-Ab prevalence in the Region (7,8). HCV-Ab prevalence levels in Egypt show a wide range across

region, age group and sex, and range from 0% to about 50% with a median of 13% (5). One major historical contributor to the high HCV-Ab prevalence observed in Egypt is the sharing of needles and syringes during the mass parenteral antischistosomal therapy campaigns conducted intensively during the 1960s and 1970s (5,7). However, other modes of exposure to HCV infection are currently driving the ongoing transmission of the infection (4,5,9).

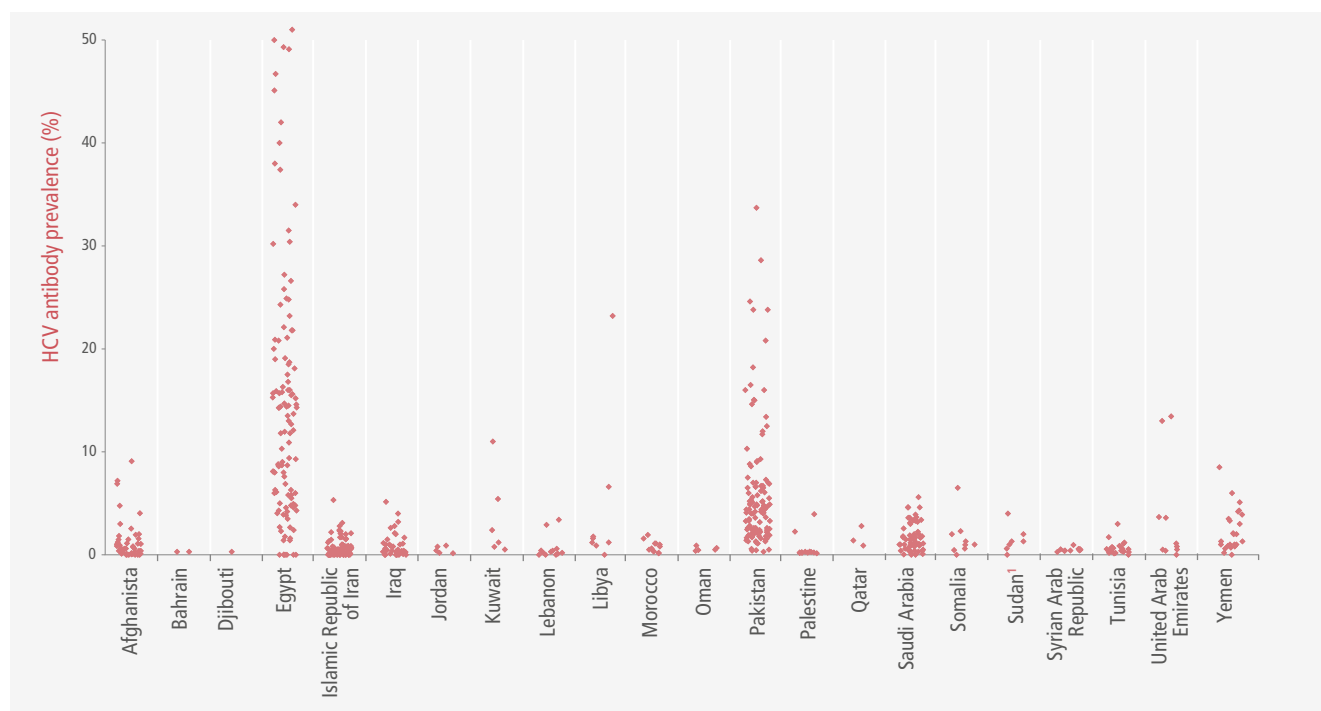


Fig 12. HCV-Ab prevalence among the general population in countries of the Region

1. Available data for Sudan before 2011, the year of independence of South Sudan, may have come from both Sudan and the newly independent Republic of South Sudan.

Pakistan also has a relatively high HCV-Ab prevalence in the general population. Here, the national HCV-Ab prevalence was assessed at 4.9% in a nationally-representative household-based prevalence survey conducted in 2007–2008 and which included children and older adults above 60 years of age (10). Overall, studies of HCV-Ab prevalence in Pakistan show a range of infection levels, from as low as 0.3% to as high as 34% with a median of 4.4% (Fig. 12) (10–12). The high HCV-Ab prevalence in Pakistan appears to be driven by diverse exposures such as sharing of injection equipment and less than optimal infection control in medical settings (10–12).

For the rest of the countries, a relatively low HCV-Ab prevalence was generally observed with most of studies showing prevalence levels of less than 3%, comparable to those observed in most countries globally (13–15). Although a few studies reported high HCV-Ab prevalence among the general population in some countries, these studies are not likely to be representative of the prevalence

in the general population in these countries (Fig. 12). The overwhelming evidence indicates that HCV-Ab prevalence among the general population in these countries is below 3%, and most often around 1%.

Fig. 13 shows HCV-Ab prevalence among different general population groups across the Region. HCV-Ab prevalence ranged from 0% to 12.1% with a median of 1% among children, from 0% to 1.3% with a median of 0.5% among antenatal clinic attendees, from 0% to 19.0% with a median of 4.2% among pregnant women, from 0% to 27.2% with a median of 1% among blood donors, from 0.4% to 4.7% with a median of 2.2% among army recruits, from 0% to 5.2% with a median of 0.3% among college students, and from 0% to 28.6% with a median of 3.2% among other general populations. Apart from the general population groups in Egypt and Pakistan, HCV-Ab prevalence levels were relatively low and consistent with global levels among the various general populations across the countries.

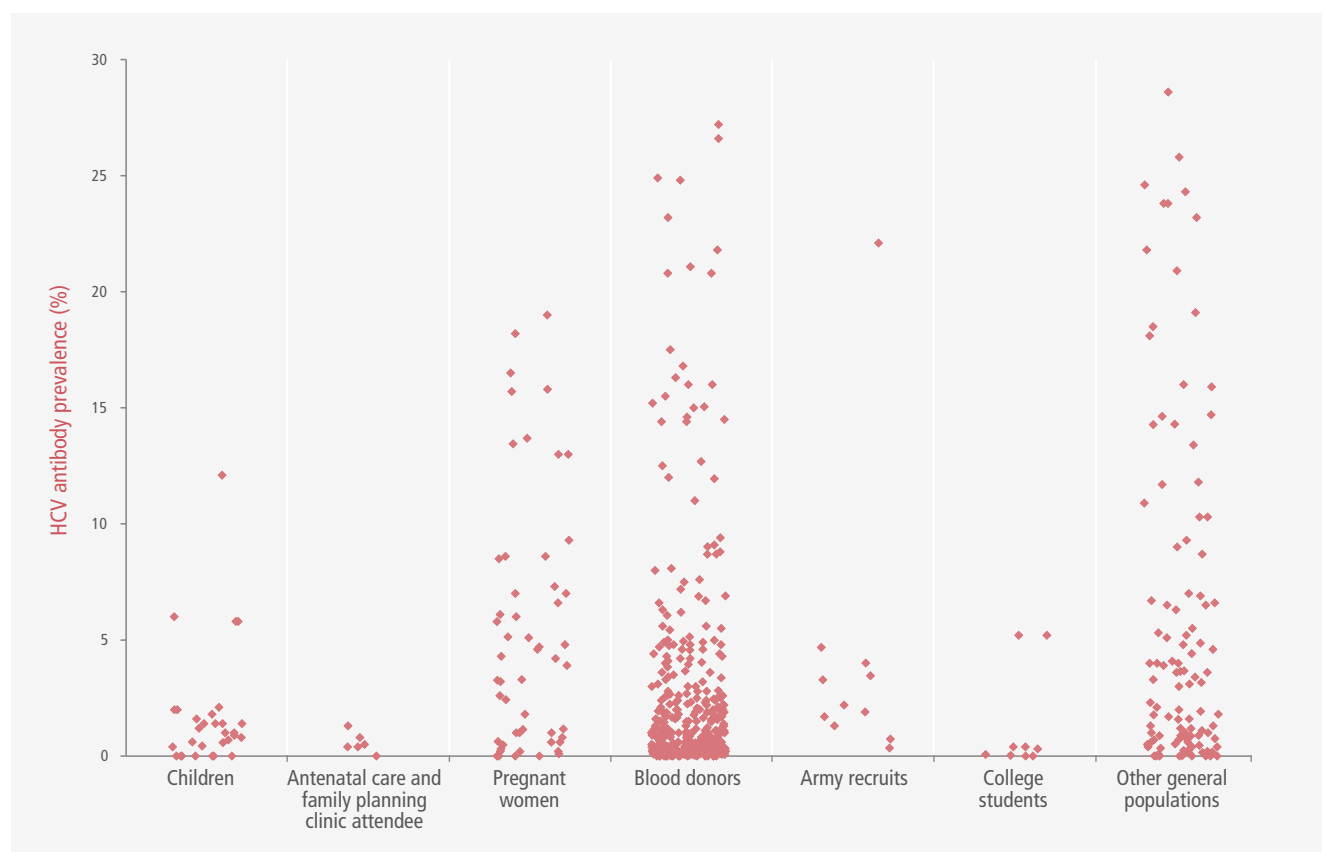


Fig 13. HCV-Ab prevalence among various general population groups in the Region

Estimates of mean HCV-Ab prevalence among the general population

Table 9 and Fig. 14 show the estimates of the mean HCV-Ab prevalence among the general population generated through meta-analyses of available HCV data for each country. The highest mean HCV-Ab prevalence among the general population was estimated for Egypt at 11.9% (95% CI: 11.2–12.6%) followed by Pakistan at 5.3% (95% CI: 4.7–5.9%). The estimated mean HCV-Ab prevalence among the general population for the rest of the countries was less than 3% and most often in the range of 1% (Table 9 and Fig. 14).

**Table 9.** Estimates of HCV-Ab prevalence among the general population in countries of the Region

| Country | Number of studies | Total sample size | HCV-Ab prevalence | | | |
|--|-------------------|-------------------|-------------------|------------|-----------------------|--|
| | | | Range (%) | Median (%) | Mean ¹ (%) | 95% confidence interval ¹ (%) |
| Afghanistan | 46 | 749 455 | 0–7.2 | 0.6 | 0.7 | 0.6–0.9 |
| Bahrain (nationals and expatriates) ² | 2 | 21 125 | 0.3–0.3 | 0.3 | 0.3 | 0.2–0.4 |
| Djibouti | 1 | 8 057 | 0.3 | 0.3 | 0.3 | 0.1–0.4 |
| Egypt | 262 | 1 672 652 | 0–57.6 | 11.6 | 11.9 | 11.2–12.6 |
| Islamic Republic of Iran | 113 | 16 288 019 | 0–3.1 | 0.3 | 0.3 | 0.2–0.4 |
| Iraq | 92 | 1 854 200 | 0–7.2 | 0.3 | 0.2 | 0.2–0.3 |
| Jordan | 12 | 126 152 | 0–2 | 0.2 | 0.3 | 0.1–0.5 |
| Kuwait (nationals) | 9 | 12 853 | 0–0.7 | 0.4 | 0.4 | 0.3–0.6 |
| Kuwait (nationals and expatriates) | 22 | 44 772 | 0–14.0 | 0.7 | 1.5 | 0.8–2.3 |
| Lebanon | 16 | 38 059 | 0–3.4 | 0.25 | 0.2 | 0.1–0.3 |
| Libya | 7 | 1 076 965 | 0.9–6.6 | 1.4 | 3.4 | 2.4–4.6 |
| Morocco | 11 | 417 897 | 0.2–1.9 | 0.8 | 0.7 | 0.4–1.1 |
| Oman (nationals and expatriates) | 6 | 64 530 | 0.4–1.0 | 0.6 | 0.4 | 0.3–0.5 |
| Pakistan | 115 | 1 739 944 | 0.3–49.0 | 4.4 | 5.3 | 4.7–5.9 |
| Palestine | 59 | 370 566 | 0–4.0 | 0.2 | 0.2 | 0.2–0.3 |
| Qatar (nationals) | 2 | 29 764 | 0.5 | 0.5 | 0.5 | 0.4–0.6 |
| Qatar (nationals and expatriates) | 16 | 153 704 | 0.3–11.2 | 0.5 | 1.1 | 0.5–1.8 |
| Saudi Arabia (nationals) | 57 | 813 230 | 0.1–9 | 1.2 | 1.7 | 1.4–1.9 |
| Saudi Arabia (nationals and expatriates) | 124 | 996 763 | 0–34 | 1.4 | 1.7 | 1.5–1.9 |
| Somalia | 9 | 14 081 | 0–6.5 | 1 | 0.9 | 0.3–1.9 |
| Sudan ³ | 7 | 1 856 | 0–4 | 1.3 | 0.9 | 0.3–1.9 |
| Syrian Arab Republic | 17 | 1 114 550 | 0.3–0.9 | 0.4 | 0.4 | 0.4–0.5 |
| Tunisia | 24 | 760 041 | 0.1–3.0 | 0.6 | 0.5 | 0.3–0.7 |
| United Arab Emirates (nationals) ² | 2 | 1 432 | 0–0.4 | 0.2 | 0.2 | 0.02–0.6 |
| United Arab Emirates (nationals and expatriates) | 11 | 290 778 | 0–36.3 | 0.5 | 1.6 | 1.0–2.5 |
| Yemen | 24 | 48 343 | 0–8.5 | 1.3 | 1.9 | 1.4–2.6 |

1. Estimates were generated by summarizing the collective evidence for HCV-Ab prevalence levels using meta-analyses applied to each country.

2. For countries where only two studies were available, HCV-Ab prevalence was estimated using the average of prevalence measures reported in these studies.

3. Available data for Sudan before 2011, the year of independence of South Sudan, may have come from both Sudan and the newly independent Republic of South Sudan.

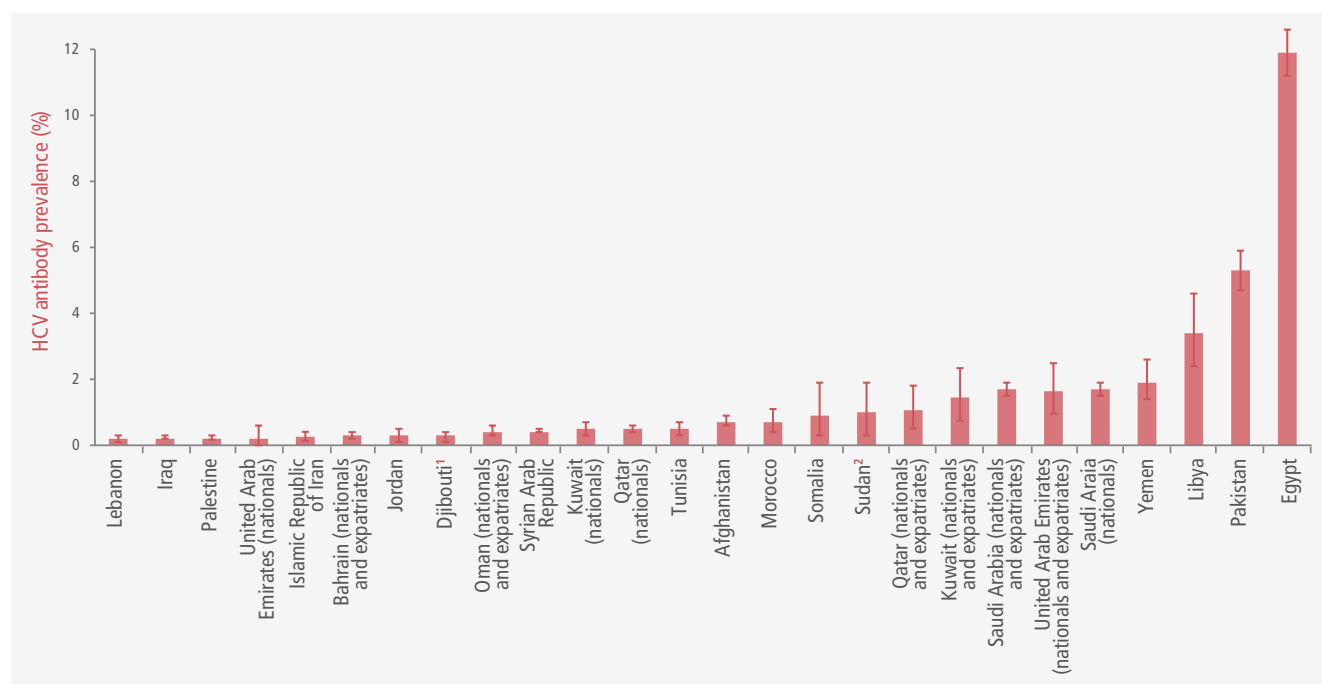


Fig 14. Estimates of the mean HCV-Ab prevalence with the corresponding 95% confidence interval among the general population in countries of the Region

1. HCV-Ab prevalence based on a single study.
2. Available data for Sudan before 2011, the year of independence of South Sudan, may have come from both Sudan and the newly independent Republic of South Sudan.

Key highlights

- Among the general population, Egypt and Pakistan are the countries most affected by HCV infection in the Region.
- HCV-Ab prevalence among the general population exceeds 10% in Egypt and is about 5% in Pakistan.
- HCV-Ab prevalence among the general population in the rest of the countries is below 3% and most often in the range of 1%. It is also comparable to global levels.

7.

Modes of exposure to HCV infection in the WHO Eastern Mediterranean Region

41 ▪ Context of HCV transmission in the Region

42 ▪ Evidence for acquisition of HCV infection through exposure in health care settings

43 ▪ Evidence for acquisition of HCV infection through community-related and informal health care exposures

▪ Evidence for acquisition of HCV infection through mother-to-child transmission

▪ Key highlights

61 ▪ References





7.

Modes of exposure to HCV infection in the WHO Eastern Mediterranean Region

41

Modes of exposure to HCV infection in the WHO Eastern Mediterranean Region

+

This section provides an overview of the various modes of HCV transmission in the Region including exposures in health care settings, exposures in the informal health care sector, exposures through community-based or traditional practices and transmission of HCV from an infected mother to her new born. HCV transmission through injecting drug use is not covered in this section as it has been discussed in Section 4 of this report.

Context of HCV transmission in the Region

The Region has been affected by several major events of parenteral transmission of bloodborne infections – that is the transmission of pathogens through blood exposures such as injections. The world's largest intravenous transmission of bloodborne infections happened in Egypt during the parenteral antischistosomal therapy mass campaigns (1,2). Millions of people were treated for schistosomiasis with intravenous injections of tartar emetic between the 1950s and 1980s, before an oral drug, praziquantel, replaced this standard of care across the country in the 1980s (1). Reuse of glass syringes and relaxed sterilization practices during these campaigns led to a large reservoir of HCV infection among the general population (Section 6) (3–5). The largest nosocomial outbreak of HIV also happened in Region, in Libya, where

402 children, 19 mothers and 2 nurses acquired the infection at a children hospital (6–8). Two other HIV outbreaks have been reported in haemodialysis centres in Egypt (9,10). High levels of incidence of HCV infection have been also observed in health care settings in different countries (Section 3).

The Region has the highest rate of injections of all WHO regions with an average of 4.3 injections per person per year (11). WHO estimates that contaminated injections are responsible for between 41 000 and 81 000 new HCV infections in the Region (12). These account for about one third of incident HCV infections attributable to contaminated injections worldwide (12). A large number of these injections are unnecessary, but are in some cases being administered because of people's preference for receiving injections over other types of equally effective therapies (13,14). There is also evidence of blood transfusions being performed even when not medically indicated (15).



Although there have been major improvements in the implementation of infection control and safety measure in health care facilities in the Region in recent years, these have not been uniform across the countries. In the Islamic Republic of Iran, the implementation of blood donor screening reduced HCV-Ab prevalence among thalassaemia patients in one study from 22.8% to 2.6% (16), while the implementation of strict infection control protocols reduced HCV-Ab prevalence among haemodialysis patients in another study from 14.4% to 4.5% (17).

Health care systems in several countries, such as Afghanistan, Pakistan, Somalia, Syrian Arab Republic and Yemen, are over-stretched leading to gaps in the implementation of safety measures including screening of all blood donations, sterilization of medical equipment and single use of needles and syringes (18–27). In Egypt, an assessment of infection control practices reported deficiencies in controlling nosocomial infections and a shortage in critical basic supplies such as antiseptics, gloves, masks, gowns and disposable syringes (28). Occupational exposures to bloodborne infections have been also documented among health care workers in the Region with the prevalence of needle-stick injuries in the previous year being reported at 48.6% in Egypt (27), 58.9% in Morocco (29) and 45% in Pakistan (26). Gaps in the implementation of standard precautionary measures appear to be more common in private practices such as among dentists (30,31). In several countries, the ongoing political and military conflicts add many challenges to the implementation of strict infection control, especially with the shortages in trained health care workers, medical supplies, and electricity and water supplies (32–36).

Other vulnerability factors for HCV transmission in the countries relate to unsafe practices at the community level. Injections by non-medical providers appear to be common (37–39). Traditional practices such as *hijamah*, or bloodletting procedures, are also common and have been linked to HCV (40,41) and HIV (42) infections in the Region. Sharing of personal hygiene belongings has been

documented in countries. For example, about one out of five university students in Afghanistan (43) and one out of three students in Sudan (44) reported sharing shaving sets. Close to 20% of military personnel in Sudan also reported sharing of shaving sets and blades (44). Certain professions, such as barbers, have been associated with a higher potential for HCV acquisition and transmission given the risk of accidental exposures to infected blood. In Morocco, HCV-Ab prevalence among barbers was five times higher than that among the general population (45) (Sections 5 and 6). Studies among traditional barbers in Morocco and Pakistan have also shown that barbers and their clients did not know about the risk of bloodborne infectious diseases and that hygiene conditions were deficient (45,46). This is of concern also because there is a tradition in some countries of barbers practising medical care and performing circumcisions (45,47).

Evidence for acquisition of HCV infection through exposure in health care settings

The review of all data sources included in this report identified hundreds of studies reporting specific risk factors for HCV infection. Studies from Egypt found a strong link between the mass campaigns for the treatment of schistosomiasis using intravenous injections and HCV infection (48–65). Across countries, HCV infection has been most often associated with exposure in health care settings such as dialysis (66–94), blood transfusion or transfusion of blood-related products (48,53–56,61,62,66,68,69,73,74,76,79,80,87,89,95–116), surgery (55,60,94,103,104,106,114,117–121), frequent injections (54,62,106,122) and dental procedures (54,62,65,103,104,118–120,123,124). Exposure to infected blood or contaminated equipment at the workplace was also a risk factor for HCV infection among health care workers (48,125).



Evidence for acquisition of HCV infection through community-related and informal health care exposures

HCV infection in the Region has been linked to unsafe practices in the community. These include the use of infected needles and contaminated sharp objects while shaving at community barbers (55,121,126) and during tattooing (95,103,124), ear piercing (103,124), circumcision (103,116), female genital mutilation (116), and bloodletting (*hijama*) (50,95). Most of these practices are performed by traditional and non-licensed practitioners in the community (5,18,127,128). The link between having an infected family member and acquiring HCV infection has been also reported in several studies (85,105,113,120,129).

Evidence for acquisition of HCV infection through mother-to-child transmission

One of the modes of HCV transmission is mother-to-child transmission, or vertical transmission. A recent systematic review reported the risk of HCV infection among infants born to mothers with chronic HCV infection at 5.8% (130). In the Region, mother-to-child transmission has been documented in several cohort studies (105,131–134). There are currently no estimates of the number of HCV infections that are due to mother-to-child transmission in countries other than Egypt. In Egypt, it has been estimated that between 3 000 and 5 000 HCV infections occur every year from mothers passing the infection to their infants (135). Mother-to-child transmission, however, is not likely to be a major route of HCV infection transmission in most countries other than Egypt and Pakistan, since HCV-Ab prevalence among the general population of women of reproductive age is not high (Section 6).

Key highlights

- HCV transmission in the Region appears to be mainly linked to poor infection control in health care settings and to the use of infected needles and contaminated sharp objects in the community.
- Mother-to-child transmission is contributing to new HCV infections in Egypt and Pakistan, but its contribution in other countries is substantially lower because of the lower HCV-Ab prevalence among women of reproductive age.



8.

Analytical insights into HCV transmission dynamics in the WHO Eastern Mediterranean Region

45

- Overview of HCV epidemiology in the Region

46

- Gaps in available evidence
- Recommendations for a better understanding of HCV epidemiology in the WHO Eastern Mediterranean Region

70

- References





8.

Analytical insights into HCV transmission dynamics in the WHO Eastern Mediterranean Region

Section 8 discusses the analytical insights reached based on the evidence-based epidemiological synthesis and analysis of HCV data among the different at-risk populations that has been presented in previous sections.

Overview of HCV epidemiology in the Region

Substantial HCV-Ab prevalence levels were found among populations with liver-related conditions in the Region indicating that HCV infection is a major cause of liver disease in this region (Section 3). High HCV-Ab incidence and prevalence levels were also observed among populations with high risk health care exposures to HCV in the Region (Section 3), notably those exposed to haemodialysis and blood transfusions (Sections 3 and 7). Elevated HCV-Ab prevalence was also found among other populations linked to health care such as hospitalized populations and patients with diabetes (Sections 5 and 7). Although some of the prevalent HCV infections may date to times before the enforcement of blood screening and strict infection control protocols across countries, the findings of this synthesis suggest that a considerable proportion of incident HCV infections are arising from less than optimal infection

control in health care settings. However, the actual number of HCV infections acquired in medical settings across the Region is not known.

Nearly half of PWID in the Region are HCV-infected, with HCV-Ab prevalence exceeding 60% in several settings across the Region (Section 4). This is not surprising considering the high levels of injecting risk behaviour, most importantly the sharing of unsterile needles and syringes, among PWID in the Region. However, with PWID constituting only 0.15% of the total population of the Region, injecting drug use is unlikely to be the dominant mode of HCV transmission in most countries, unlike in some of the developed countries such as the United States (1–3). Substantial HCV-Ab prevalence levels were also found among prisoners in countries, probably because of injecting drug use during or before incarceration, and possibly because of other risk behaviours such as tattooing and unprotected anal sex (Section 5).



Two countries of the Region are most affected by HCV infection, namely Egypt where the national HCV-Ab prevalence is about 10% and Pakistan where the national HCV-Ab prevalence is about 5% (Section 6). For the other countries, HCV-Ab prevalence among the general population is below 3% and most often about 1%, which is comparable to most countries globally.

The risk factors for HCV infection identified through this synthesis (Section 7) confirm the HCV epidemiology patterns observed among the different at-risk populations in the Region. The main driver of HCV infection transmission in the Region appears to be the less than optimal infection control in health care settings. HCV transmission also occurs through informal health care exposure in the community, for example through the use of unsterile needles/syringes for medical injections and contaminated sharp objects for minor surgical procedures such as bloodletting and circumcision. The contribution of community-based exposures to incidence of HCV infection in the different countries remains unknown. HCV is also transmitted through mother-to-child transmission which is an important contributor to incidence of HCV infection in Egypt and also possibly in Pakistan, but unlikely to be so in other countries.

Gaps in available evidence

The extensive literature reviews of the HCV Epidemiology Synthesis Project identified several gaps in available evidence for HCV epidemiology across the Region. For example, there are no studies assessing HCV infection among populations with high risk health care exposure to HCV in some countries. Data on PWID and other vulnerable populations, such as prisoners, are also limited in many countries. Geographical heterogeneity in HCV-Ab prevalence has been noted within countries, such as in Egypt (4) and Pakistan (5), and it is possible that many studies were conducted in areas of higher rather than lower HCV-Ab prevalence. This may have affected the representativeness of HCV estimates at the national level. There are currently no sufficiently precise estimates of the number of new HCV infections occurring every year across the Region. There are also not sufficient data to estimate the contribution of the different modes of exposures to the total number of new HCV infections arising across the Region.

Recommendations for a better understanding of HCV epidemiology in the WHO Eastern Mediterranean Region

Further scientific research is necessary to develop a better understanding of HCV epidemiology in the Region and to inform public health policy and programming as well as resource allocation in this Region. Nationally-representative population-based surveys are needed to measure HCV-Ab prevalence in the population, delineate the spatial variability in prevalence, identify specific modes of exposure and assess HCV knowledge and attitudes in each country of the Region, as has been done recently in Egypt and Pakistan (5,6). Repeated prevalence surveys are also desirable and can be used in combination with mathematical modelling to estimate incidence of HCV infection as well as the contribution of various sources of exposure to new HCV infections. The expansion of HCV research into populations with high risk health care exposure and other vulnerable populations such as PWID and prisoners is essential.

The present analysis provides evidence of the extent of HCV infection in the Region among certain populations and subpopulations. It shows that HCV infection is a significant health problem across the Region among certain populations and among the general population in two countries. It is also a major cause of liver disease in the Region. Countries of the Region need to take action to tackle HCV infection as well as the overall burden of viral hepatitis.

9.

Responding to viral hepatitis with a focus on HCV infection across the WHO Eastern Mediterranean Region: the way forward

48

▪ Setting the context

49

▪ Status of national responses in 2016 across the Region

50

▪ The way forward

70

▪ References





9.

48

Responding to viral hepatitis with a focus on HCV infection across the WHO Eastern Mediterranean Region: the way forward

Responding to viral hepatitis with a focus on HCV infection across the WHO Eastern Mediterranean Region: the way forward



Section 9 presents an overview of the national response to viral hepatitis in countries with a focus on HCV infection. Opportunities for scaling up viral hepatitis response in the Region to achieve HCV elimination by 2030 are also discussed.

Setting the context

Viral hepatitis epidemiology, health system capacity and resource availability vary widely across the Region. Eliminating viral hepatitis in this region requires that each country sets its own evidence-informed national response to effectively achieve prevention of new infections, treatment of chronic infections and control of hepatitis

disease sequelae, namely liver cirrhosis and liver cancer. To be effective, the national response will need to take account of the needs and priorities of the people living with viral hepatitis and the populations at risk of infection, as well as the characteristics and capacity of the health sector and the financial resources that can be made available for response implementation.



Status of national responses in 2016 across the Region

While HIV programmes in the Region have made a considerable progress in recent years, programmes to control viral hepatitis, with the exception of hepatitis B virus childhood vaccination, have not received adequate attention in most countries. In 2016, the WHO Regional Office for the Eastern Mediterranean conducted a regional questionnaire survey to review the status of hepatitis response in each of its 22 countries. Sixteen countries responded and all except one country had prevention and care interventions for viral hepatitis in place, although implementation of the interventions was limited in scope and scale. Approaches to prevention and treatment were found to be very considerably across countries.

Although 13 countries reported having a strategy or plan for the prevention and control of viral hepatitis, baseline data on the levels of HCV infection, the main routes of transmission and coverage of prevention and treatment services were not available for most countries. This points to a serious lack in concrete targets for reducing the levels of infection and burden of disease and for increasing service coverage in most national hepatitis plans.

Access to care and treatment services remains problematic in most countries. Case detection of chronic HCV and hepatitis B virus infections continues to be very low even in countries where viral hepatitis programmes are in place. The majority of affected individuals are unaware of their infection until late disease stages, further complicating disease progression and treatment options. The poor access to care and treatment in early infection stages suggests that infected individuals remain a source of onward infection transmission in the population.

Improving hepatitis case detection entails first prioritizing screening for populations at higher risk of exposure. Analysis of epidemiological data from prevalence surveys, such as that presented in this report, as well as from hepatitis case notifications and screening programmes,

provides insight into which population groups are at higher risk of exposure to HCV and, with the exception of hepatitis B virus childhood vaccination, programmes to control viral hepatitis have not received due attention in most countries. The standardization and simplification of screening procedures will contribute to a wider coverage of screening services.

Ensuring the continued engagement of viral hepatitis patients along the continuum of care has also been challenging, especially for countries with weak health systems. High out-of-pocket payments required from patients are a major barrier to accessing viral hepatitis diagnosis and treatment in many countries. Providing access to HCV treatment with the new direct-acting antivirals (DAAs) has been particularly challenging. Since late 2014, remarkable efforts have been made in Egypt and Pakistan to increase access to DAAs. It is reported that well over 1 000 000 people have received treatment with DAAs in Egypt⁴ and at least 80 000 in Pakistan (1). In view of the high number of people with chronic HCV infection in these countries, continued extensive testing and treatment scale-up will be required to reduce the burden of liver disease. Scale-up of DAA treatment in other countries continues to be slow.

One of the main reasons for poor access and limited treatment coverage is the cost of HCV treatment. Although DAAs have been adopted in HCV treatment protocols across countries and some few countries have been able to reduce the cost tremendously, the costs are still prohibitive and unsustainable for some countries, regardless of whether the cost is covered by government, health insurance or out-of-pocket payments of patients.

As highlighted in this report, many countries lack strategic information on the local epidemiology of viral hepatitis and on the expected impact and cost-effectiveness of different prevention and care interventions. This is a contributing factor to low national commitment and domestic investment in the viral hepatitis response. Studies to assess epidemiological impact and health economics of scale-up of prevention and treatment services are critical

4. Presentation made at the WHO Regional Office for the Eastern Mediterranean on 20 March 2017.

5. Information provided to the WHO Regional Office for the Eastern Mediterranean by hepatitis focal points in ministries of health, 2016.



to inform policy and resource allocation, and to advocate for an effective national viral hepatitis response.

Currently several countries in the Region are affected by protracted emergencies. Millions of people have been displaced and this has drawn attention to emergency relief efforts, as opposed to other health priorities. Affected countries have had to delay scale-up efforts of health sector programmes including viral hepatitis programmes. Meanwhile, the large populations of displaced people continue to have limited access to hepatitis prevention, diagnosis and treatment services.

The way forward

WHO has led the development of the first *Global health sector strategy on viral hepatitis, 2016–2021*, with elimination of viral hepatitis as a public health threat by 2030 as its central goal (2). The strategy is closely aligned with the 2030 Agenda for Sustainable Development and the health targets of the Sustainable Development Goals (SDGs), in particular SDG 3, which calls for specific action to combat viral hepatitis and achieve universal health coverage; and specific action to related global health strategies and plans, including those for HIV, sexually transmitted infections, blood safety and noncommunicable diseases.

The global strategy for viral hepatitis provides:

- A vision of a world where viral hepatitis transmission is halted and everyone living with viral hepatitis has access to safe, affordable and effective care and treatment;
- A goal of eliminating viral hepatitis as a major public health threat by 2030; and
- Targets that seek to reduce the number of newly occurring chronic HCV and hepatitis B virus infections from the current 6–10 million cases to 0.9 million cases per year by 2030, and to reduce the annual deaths from chronic viral hepatitis from 1.4 million to less than 0.5 million by 2030, with milestones for 2020.

Based on the WHO global strategy for viral hepatitis, the WHO Regional Office for the Eastern Mediterranean developed a *Regional action plan for the implementation of the Global health sector strategy for viral hepatitis 2017–2021* in consultation with hepatitis focal points

of ministries of health, regional hepatitis experts and academic researchers, civil society representatives, and experts from WHO partner agencies (3). Recommendations for priority actions were based on infection levels and burden of disease and its variation between countries, and between populations within countries, and factored in gaps in existing programmes and resources.

The regional action plan is intended to guide Member States and the WHO Secretariat on priority actions towards the achievement of national, regional and global targets. It calls for involving stakeholders from the public and private sectors and civil society in viral hepatitis response, strengthening governance and public policy, generating data to better understand viral hepatitis epidemics and epidemiological impact and the health economics of interventions, enhancing prevention strategies, and improving access to affordable screening, diagnosis and treatment of HCV and hepatitis infections.

The regional action plan focuses on five key interventions for scale-up:

1. Hepatitis B vaccination (including birth dose);
2. Safe injection practices and safe blood;
3. Harm reduction for PWID;
4. Hepatitis B treatment;
5. HCV cure.

Actions to facilitate scale-up of these key interventions are outlined in the strategy under five strategic directions, including leadership/good governance, strategic information, service delivery, health systems strengthening and financing for sustainability.

The regional action plan will be implemented in a phased manner with different starting points for different countries depending on the status of the response to viral hepatitis in 2016. The speed of scale up of the response will depend on several key factors: infection levels and disease burden, political commitment, economic and health systems capacity, and the impact of protracted emergencies in the Region on health sector priorities. The regional action plan proposes programmatic milestones for 2018 and 2021. If adopted by each country, the achievement of these milestones will result in tangible progress towards the global goal of eliminating HCV and hepatitis B infections by 2030.



References

1. Introduction

Stanaway JD, Flaxman AD, Naghavi M, Fitzmaurice C, Vos T, Abubakar I, et al. The global burden of viral hepatitis from 1990 to 2013: findings from the Global Burden of Disease Study 2013. *Lancet*. 2016 Sep 10;388(10049):1081–8. [http://dx.doi.org/10.1016/S0140-6736\(16\)30579-7](http://dx.doi.org/10.1016/S0140-6736(16)30579-7) PMID:27394647.

1. Choo QL, Kuo G, Weiner AJ, Overby LR, Bradley DW, Houghton M. Isolation of a cDNA clone derived from a blood-borne non-A, non-B viral hepatitis genome. *Science*. 1989 Apr 21;244(4902):359–62. <http://dx.doi.org/10.1126/science.2523562> PMID:2523562.
2. Kuo G, Choo QL, Alter HJ, Gitnick GL, Redeker AG, Purcell RH, et al. An assay for circulating antibodies to a major etiologic virus of human non-A, non-B hepatitis. *Science*. 1989 Apr 21;244(4902):362–4. <http://dx.doi.org/10.1126/science.2496467> PMID:2496467.
3. Mohd Hanafiah K, Groeger J, Flaxman AD, Wiersma ST. Global epidemiology of hepatitis C virus infection: new estimates of age-specific antibody to HCV seroprevalence. *Hepatology*. 2013 Apr;57(4):1333–42. <http://dx.doi.org/10.1002/hep.26141> PMID:23172780.
4. Global hepatitis report 2017. Geneva: World Health Organization; 2017 (<https://apps.who.int/iris/handle/10665/255016>, accessed 14 June 2020).
5. Chen SL, Morgan TR. The natural history of hepatitis C virus (HCV) infection. *Int J Med Sci*. 2006;3(2):47–52. <http://dx.doi.org/10.7150/ijms.3.47> PMID:16614742.
6. Ly KN, Xing J, Klevens RM, Jiles RB, Holmberg SD. Causes of death and characteristics of decedents with viral hepatitis, United States, 2010. *Clin Infect Dis*. 2014 Jan;58(1):40–9. <http://dx.doi.org/10.1093/cid/cit642> PMID:24065331.
7. Mahajan R, Xing J, Liu SJ, Ly KN, Moorman AC, Rupp L, et al.; Chronic Hepatitis Cohort Study (CHeCS) Investigators. Mortality among persons in care with hepatitis C virus infection: the Chronic Hepatitis Cohort Study (CHeCS), 2006–2010. *Clin Infect Dis*. 2014 Apr;58(8):1055–61. <http://dx.doi.org/10.1093/cid/ciu077> PMID:24523214.
8. Hajarizadeh B, Grebely J, Dore GJ. Epidemiology and natural history of HCV infection. *Nat Rev Gastroenterol Hepatol*. 2013 Sep;10(9):553–62. <http://dx.doi.org/10.1038/nrgastro.2013.107> PMID:23817321.
9. University of Washington. Hepatitis C diagnostic testing. 2017 (www.hepatitisc.uw.edu/pdf/screening-diagnosis/diagnostic-testing/core-concept/all, accessed 8 July 2019).



10. World Health Organization. Media centre. Hepatitis C: fact sheet. Updated July 2017 (www.who.int/mediacentre/factsheets/fs164/en/, accessed 8 July 2019).
11. Centers for Disease Control and Prevention. Hepatitis C. (<https://wwwnc.cdc.gov/travel/yellowbook/2018/infectious-diseases-related-to-travel/hepatitis-c>, accessed 8 July 2019).
12. Alter MJ. Epidemiology of hepatitis C virus infection. *World J Gastroenterol*. 2007 May 7;13(17):2436–41. <http://dx.doi.org/10.3748/wjg.v13.i17.2436> PMID:17552026.
13. Benova L, Mohamoud YA, Calvert C, Abu-Raddad LJ. Vertical transmission of hepatitis C virus: systematic review and meta-analysis. *Clin Infect Dis*. 2014 Sep 15;59(6):765–73. <http://dx.doi.org/10.1093/cid/ciu447> PMID:24928290.
14. A special meeting review edition: advances in the treatment of hepatitis C virus infection from EASL 2015: The 50th Annual Meeting of the European Association for the Study of the Liver, April 22–26, 2015, Vienna, Austria. *Gastroenterol Hepatol*. 2015;11(6) Suppl 3:1–23. PMID: 26504459.
15. Global health sector strategy on viral hepatitis, 2016–2021. Geneva: World Health Organization; 2015.
16. Combating hepatitis B and C to reach elimination by 2030. Geneva: World Health Organization; 2016:1–17.
17. Technical considerations and case definitions to improve surveillance for viral hepatitis. Geneva: World Health Organization; 2015.
18. Manual for the development and assessment of national viral hepatitis plans: a provisional document. Geneva: World Health Organization; 2015:50.
19. Monitoring and evaluation for viral hepatitis B and C: recommended indicators and framework. Geneva: World Health Organization; 2016.
20. Ministry of Health and Population, Egypt, El-Zanaty and Associates, and ICF International. Egypt health issues survey 2015. Cairo, Egypt and Rockville, Maryland: Ministry of Health and Population and ICF International; 2015.
21. Mohamoud YA, Mumtaz GR, Riome S, Miller D, Abu-Raddad LJ. The epidemiology of hepatitis C virus in Egypt: a systematic review and data synthesis. *BMC Infect Dis*. 2013 Jun 24;13(1):288. <http://dx.doi.org/10.1186/1471-2334-13-288> PMID:23799878.
22. El-Zanaty F, Way A. Egypt demographic and health survey 2008. Cairo: Ministry of Health, El-Zanaty and Associates, and Macro International; 2009.
23. Qureshi H, Bile KM, Jooma R, Alam SE, Afridi HU. Prevalence of hepatitis B and C viral infections in Pakistan: findings of a national survey appealing for effective prevention and control measures. *East Mediterr Health J*. 2010;16 Suppl:S15–23. PMID:21495584.
24. Umar M, Bushra HT, Ahmad M, Data A, Ahmad M, Khurram M, et al. Hepatitis C in Pakistan: a review of available data. *Hepat Mon*. 2010 Summer;10(3):205–14. PMID:22308140.
25. Chaabna K, Mohamoud YA, Chemaitelly H, Mumtaz GR, Abu-Raddad LJ. Protocol for a systematic review and meta-analysis of hepatitis C virus (HCV) prevalence and incidence in the Horn of Africa sub-region of the Middle East and North Africa. PROSPERO International prospective register of systematic reviews (http://www.crd.york.ac.uk/prospere/display_record.asp?ID=CRD42014010318, accessed 8 July 2019).
26. Mahmud S, Akbarzadeh V, Abu-Raddad LJ. The epidemiology of hepatitis C virus in Iran: Systematic review and meta-analyses. Unpublished results.



27. Benova L, Awad SF, Miller FD, Abu-Raddad LJ. Estimation of hepatitis C virus infections resulting from vertical transmission in Egypt. *Hepatology*. 2015 Mar;61(3):834–42. <http://dx.doi.org/10.1002/hep.27596> PMID:25366418.
28. Chemaitelly H, Mahmud S, Rahmani AM, Abu-Raddad LJ. The epidemiology of hepatitis C virus in Afghanistan: systematic review and meta-analysis. *Int J Infect Dis*. 2015 Nov;40:54–63. <http://dx.doi.org/10.1016/j.ijid.2015.09.011> PMID:26417880.
29. Mohamoud YA, Riome S, Abu-Raddad LJ. Epidemiology of hepatitis C virus in the Arabian Gulf countries: Systematic review and meta-analysis of prevalence. *Int J Infect Dis*. 2016 May;46:116–25. <http://dx.doi.org/10.1016/j.ijid.2016.03.012> PMID:26996460.
30. Chaabna K, Kouyoumjian SP, Abu-Raddad LJ. Hepatitis C Virus Epidemiology in Djibouti, Somalia, Sudan, and Yemen: Systematic Review and Meta-Analysis. *PLoS One*. 2016 Feb 22;11(2):e0149966. <http://dx.doi.org/10.1371/journal.pone.0149966> PMID:26900839.
31. Chemaitelly H, Chaabna K, Abu-Raddad LJ. The epidemiology of hepatitis c virus in the fertile crescent: systematic review and meta-analysis. *PLoS One*. 2015 Aug 21;10(8):e0135281. <http://dx.doi.org/10.1371/journal.pone.0135281> PMID:26296200.
32. Fadlalla FA, Mohamoud YA, Mumtaz GR, Abu-Raddad LJ. The epidemiology of hepatitis C virus in the Maghreb region: systematic review and meta-analyses. *PLoS One*. 2015 Mar 24;10(3):e0121873. <http://dx.doi.org/10.1371/journal.pone.0121873> PMID:25803848.
33. Chaabna K, Mohamoud YA, Chemaitelly H, Mumtaz GR, Abu-Raddad LJ. Protocol for a systematic review and meta-analysis of hepatitis C virus (HCV) prevalence and incidence in the Horn of Africa sub-region of the Middle East and North Africa. *Syst Rev*. 2014 Dec 16;3(1):146. <http://dx.doi.org/10.1186/2046-4053-3-146> PMID:25516265.
34. Mumtaz GR, Weiss HA, Thomas SL, Riome S, Setayesh H, Riedner G, et al. HIV among people who inject drugs in the Middle East and North Africa: systematic review and data synthesis. *PLoS Med*. 2014 Jun 17;11(6):e1001663. <http://dx.doi.org/10.1371/journal.pmed.1001663> PMID:24937136.
35. The utility of estimates for health monitoring and decision-making: global, regional and country perspectives: report of a technical meeting, WHO, Glion sur Montreux, Switzerland 24–25 June 2015. Geneva: World Health Organization; 2015:1-17.

2. Research methodology and conceptual framework

1. PROSPERO International prospective register of systematic reviews. Chaabna K, Mohamoud YA, Chemaitelly H, Mumtaz GR, Abu-Raddad LJ. Protocol for a systematic review and meta-analysis of hepatitis C virus (HCV) prevalence and incidence in The Horn of Africa sub-region of the Middle East and North Africa (http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42014010318, accessed 8 July 2019).
2. Mohamoud YA, Mumtaz GR, Riome S, Miller D, Abu-Raddad LJ. The epidemiology of hepatitis C virus in Egypt: a systematic review and data synthesis. *BMC Infect Dis*. 2013 Jun 24;13(1):288. <http://dx.doi.org/10.1186/1471-2334-13-288> PMID:23799878.
3. Benova L, Mohamoud YA, Calvert C, Abu-Raddad LJ. Vertical transmission of hepatitis C virus: systematic review and meta-analysis. *Clin Infect Dis*. 2014 Sep 15;59(6):765–73. <http://dx.doi.org/10.1093/cid/ciu447> PMID:24928290.



4. Benova L, Awad SF, Miller FD, Abu-Raddad LJ. Estimation of hepatitis C virus infections resulting from vertical transmission in Egypt. *Hepatology*. 2015 Mar;61(3):834–42. <http://dx.doi.org/10.1002/hep.27596> PMID:25366418.
5. Chemaitelly H, Mahmud S, Rahmani AM, Abu-Raddad LJ. The epidemiology of hepatitis C virus in Afghanistan: systematic review and meta-analysis. *Int J Infect Dis*. 2015 Nov;40:54–63. <http://dx.doi.org/10.1016/j.ijid.2015.09.011> PMID:26417880.
6. Mohamoud YA, Riome S, Abu-Raddad LJ. Epidemiology of hepatitis C virus in the Arabian Gulf countries: Systematic review and meta-analysis of prevalence. *Int J Infect Dis*. 2016 May;46:116–25. <http://dx.doi.org/10.1016/j.ijid.2016.03.012> PMID:26996460.
7. Chaabna K, Kouyoumjian SP, Abu-Raddad LJ. Hepatitis C Virus Epidemiology in Djibouti, Somalia, Sudan, and Yemen: Systematic Review and Meta-Analysis. *PLoS One*. 2016 Feb 22;11(2):e0149966. <http://dx.doi.org/10.1371/journal.pone.0149966> PMID:26900839.
8. Chemaitelly H, Chaabna K, Abu-Raddad LJ. The Epidemiology of Hepatitis C Virus in the Fertile Crescent: Systematic Review and Meta-Analysis. *PLoS One*. 2015 Aug 21;10(8):e0135281. <http://dx.doi.org/10.1371/journal.pone.0135281> PMID:26296200.
9. Fadlalla FA, Mohamoud YA, Mumtaz GR, Abu-Raddad LJ. The epidemiology of hepatitis C virus in the Maghreb region: systematic review and meta-analyses. *PLoS One*. 2015 Mar 24;10(3):e0121873. <http://dx.doi.org/10.1371/journal.pone.0121873> PMID:25803848.
10. Chaabna K, Mohamoud YA, Chemaitelly H, Mumtaz GR, Abu-Raddad LJ. Protocol for a systematic review and meta-analysis of hepatitis C virus (HCV) prevalence and incidence in the Horn of Africa sub-region of the Middle East and North Africa. *Syst Rev*. 2014 Dec 16;3(1):146. <http://dx.doi.org/10.1186/2046-4053-3-146> PMID:25516265.
11. The Cochrane collaboration. *Cochrane handbook for systematic reviews of interventions*. Hoboken (New Jersey): Wiley-Blackwell; 2008.
12. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med*. 2009 Jul 21;6(7):e1000097. <http://dx.doi.org/10.1371/journal.pmed.1000097> PMID:19621072.
13. Choo Q-L, Kuo G, Weiner AJ, Overby LR, Bradley DW, Houghton M. Isolation of a cDNA clone derived from a blood-borne non-A, non-B viral hepatitis genome. *Science*. 1989 Apr 21;244(4902):359–62. <http://dx.doi.org/10.1126/science.2523562> PMID:2523562.
14. Kuo G, Choo QL, Alter HJ, Gitnick GL, Redeker AG, Purcell RH, et al. An assay for circulating antibodies to a major etiologic virus of human non-A, non-B hepatitis. *Science*. 1989 Apr 21;244(4902):362–4. <http://dx.doi.org/10.1126/science.2496467> PMID:2496467.
15. Borenstein M, Hedges LV, Higgins JPT, Rothstein HR. *Introduction to meta-analysis*. Chichester: John Wiley & Sons; 2009:421.



3. HCV epidemiology among populations with high risk health care exposure to HCV and populations with liver-related conditions

1. Jabbari A, Besharat S, Khodabakshi B. Hepatitis C in hemodialysis centers of golestan province, northeast of Iran (2005). *Hepat Mon.* 2008;8(1):61–5.
2. Zahran AM. Prevalence of seroconversion of hepatitis C virus among hemodialysis patients in Menoufia Governorate, Egypt. *Arab J Nephrol Transplant.* 2014 May;7(2):133–5. PMID:25366511.
3. Al-Rubaie HMM, Malik AS. Seroconversion rate of hepatitis C virus infection among haemodialysis patients in Al-Kadhimiya Teaching Hospital (dialysis unit). *Ir J Med Sci.* 2011;9(4):343–9.
4. Sekkat S, Kamal N, Benali B, Fellah H, Amazian K, Bourquia A, et al. Prévalence des anticorps anti-VHC et incidence de séroconversion dans cinq centres d'hémodialyse au Maroc [Prevalence of anti-HCV antibodies and seroconversion incidence in five haemodialysis units in Morocco]. *Nephrol Ther.* 2008 Apr;4(2):105–10. <http://dx.doi.org/10.1016/j.nephro.2007.11.007> PMID:18272446.
5. Ben Othman S, Bouzgarrou N, Achour A, Bourlet T, Pozzetto B, Trabelsi A. Prévalence et incidence élevées de l'infection par le virus de l'hépatite C chez les hémodialysés dans la région Centre-Est de la Tunisie [High prevalence and incidence of hepatitis C virus infections among dialysis patients in the East-Centre of Tunisia]. *Pathol Biol (Paris).* 2004 Jul;52(6):323–7. <http://dx.doi.org/10.1016/j.patbio.2003.07.001> PMID:15261374.
6. Soliman AR, Momtaz Abd Elaziz M, El Lawindi MI. Evaluation of an isolation program of hepatitis C virus infected hemodialysis patients in some hemodialysis centers in Egypt. *ISRN Nephrol.* 2013;2013:395467. PMID: 24967226.
7. Khodir SA, Alghateb M, Okasha KM, Shalaby Sel-S. Prevalence of HCV infections among hemodialysis patients in Al Gharbiyah Governorate, Egypt. *Arab J Nephrol Transplant.* 2012 Sep;5(3):145–7. PMID:22967252.
8. El-Sherif A, Elbahrawy A, Aboelfotoh A, Abdelkarim M, Saied Mohammad AG, Abdallah AM, et al. High false-negative rate of anti-HCV among Egyptian patients on regular hemodialysis. *Hemodial Int.* 2012 Jul;16(3):420–7. <http://dx.doi.org/10.1111/j.1542-4758.2011.00662.x> PMID:22360424.
9. Goher SA, Abdel Ghany MM, Shaarawy A-B, Sobhy SA. Dialyzer reuse and hepatitis C virus in hemodialysis population in Egypt. *Sci Med J.* 1998;10(3):43–54.
10. Azarkeivan A, Toosi MN, Maghsudlu M, Kafiabad SA, Hajibeigi B, Hadizadeh M. The incidence of hepatitis C in patients with thalassemia after screening in blood transfusion centers: a fourteen-year study. *Transfusion.* 2012 Aug;52(8):1814–8. <http://dx.doi.org/10.1111/j.1537-2995.2012.03652.x> PMID:22500658.
11. Batieha A, Abdallah S, Maghaireh M, Awad Z, Al-Akash N, Batieneh A, et al. Epidemiology and cost of haemodialysis in Jordan. *East Mediterr Health J.* 2007 May-Jun;13(3):654–63. PMID:17687839.
12. Hassan NF, el Ghorab NM, Abdel Rehim MS, el Sharkawy MS, el Sayed NM, Emara K, et al. HIV infection in renal dialysis patients in Egypt. *AIDS.* 1994 Jun;8(6):853. <http://dx.doi.org/10.1097/00002030-199406000-00023> PMID:8086148.
13. El Sayed NM, Gomatos PJ, Beck-Sagué CM, Dietrich U, von Briesen H, Osmanov S, et al. Epidemic transmission of human immunodeficiency virus in renal dialysis centers in Egypt. *J Infect Dis.* 2000 Jan;181(1):91–7. <http://dx.doi.org/10.1086/315167> PMID:10608755.
14. Visco-Comandini U, Cappiello G, Liuzzi G, Tozzi V, Anzidei G, Abbate I, et al.; Libya Project Task Force.



Monophyletic HIV type 1 CRF02-AG in a nosocomial outbreak in Benghazi, Libya. *AIDS Res Hum Retroviruses*. 2002 Jul 1;18(10):727–32. <http://dx.doi.org/10.1089/088922202760072366> PMID:12167281.

15. de Oliveira T, Pybus OG, Rambaut A, Salemi M, Cassol S, Ciccozzi M, et al.; Benghazi Study Group. Molecular epidemiology: HIV-1 and HCV sequences from Libyan outbreak. *Nature*. 2006 Dec 14;444(7121):836–7. <http://dx.doi.org/10.1038/444836a> PMID:17171825.
16. Yerly S, Quadri R, Negro F, Barbe KP, Cheseaux JJ, Burgisser P, et al. Nosocomial outbreak of multiple bloodborne viral infections. *J Infect Dis*. 2001 Aug 1;184(3):369–72. <http://dx.doi.org/10.1086/322036> PMID:11443566.
17. Askarian M, Mirzaei K, McLaws ML. Attitudes, beliefs, and infection control practices of Iranian dentists associated with HIV-positive patients. *Am J Infect Control*. 2006 Oct;34(8):530–3. <http://dx.doi.org/10.1016/j.ajic.2006.03.006> PMID:17015160.
18. Askarian M, Mirzaei K, Cookson B. Knowledge, attitudes, and practice of Iranian dentists with regard to HIV-related disease. *Infect Control Hosp Epidemiol*. 2007 Jan;28(1):83–7. <http://dx.doi.org/10.1086/509851> PMID:17230393.
19. Kabbash IA, El-Sayed NM, Al-Nawawy AN, Abou Salem Mel-S, El-Deek B, Hassan NM. Risk perception and precautions taken by health care workers for HIV infection in haemodialysis units in Egypt. *East Mediterr Health J*. 2007 Mar-Apr;13(2):392–407. PMID:17684860.
20. Mohamoud YA, Miller FD, Abu-Raddad LJ. Potential for human immunodeficiency virus parenteral transmission in the Middle East and North Africa: an analysis using hepatitis C virus as a proxy biomarker. *World J Gastroenterol*. 2014 Sep 28;20(36):12734–52. <http://dx.doi.org/10.3748/wjg.v20.i36.12734> PMID:25278675.

4. HCV epidemiology among people who inject drugs

1. Mumtaz GR, Weiss HA, Thomas SL, Riome S, Setayesh H, Riedner G, et al. HIV among people who inject drugs in the Middle East and North Africa: systematic review and data synthesis. *PLoS Med*. 2014 Jun 17;11(6):e1001663. doi.org/10.1371/journal.pmed.1001663 PMID:24937136.
2. Updated data on the size of the people who inject drug population in the Eastern Mediterranean Region. Cairo; Eastern Mediterranean Region Office of the World Health Organization; 2016.
3. HIV integrated behavioral and biological surveillance surveys- injecting drug users in Tanger and Nador, Morocco. Rabat: Ministry of Health, National STI/AIDS Programme, Joint United Nations Programme on HIV/AIDS, and Global Fund Unit; 2012.
4. Global AIDS response progress report. Kabul, Afghanistan National AIDS Control Programme; 2014.
5. Jacobson JO, Saidel TJ, Loo V. Estimating the size of key affected populations at elevated risk for HIV in Egypt, 2014. Cairo: National AIDS Program, Ministry of Health and Population with the Joint United Nations Programme on HIV/AIDS, the United National Population Fund and the United Nations Office on Drugs and Crime; 2015 (https://www.unodc.org/documents/middleeastandnorthafrica/Publications/PSE_New_-_Draft_3_-_PLANnPLAY_-_101016.pdf, accessed 8 July 2019).
6. Global AIDS response progress report. Kuwait city: Kuwait National AIDS Control Programme; 2014.
7. Global AIDS response progress report. Manama: Bahrain National AIDS Control Program; 2014.



8. Heimer R, Khoshnood K, Crawford F, Shebl F, Barbour R, Khouri D, et al. Project CROSSROADS: size estimation, risk behavior assessment, and disease prevalence in populations at high risk for HIV infection in Lebanon. Beirut: Middle East and North Africa Harm Reduction Association (MENAHRRA); 2015.
9. Populations estimation exercise based on an extrapolation of data from 2011, Bangkok: Pakistan National AIDS Programme and UNAIDS Asia-Pacific Regional Support Team; 2015.
10. Nelson PK, Mathers BM, Cowie B, Hagan H, Des Jarlais D, Horyniak D, et al. Global epidemiology of hepatitis B and hepatitis C in people who inject drugs: results of systematic reviews. *Lancet*. 2011 Aug 13;378(9791):571–83. doi.org/10.1016/S0140-6736(11)61097-0 PMID:21802134.
11. Global AIDS response progress report. Tunis: Tunisia National AIDS Control Programme; 2014.
12. Abu-Raddad LJ, Akala FA, Semini I, Riedner G, Wilson D, Tawil O. Characterizing the HIV/AIDS epidemic in the Middle East and North Africa: time for strategic action. Washington, DC: World Bank; 2010 (<http://documents.worldbank.org/curated/en/473151468052141714/pdf/548890PUB0EPI11C10Dislosed061312010.pdfm>, accessed 8 July 2019).
13. Preliminary analysis of Jordan IBBSS among injecting drug users. Amman: Jordan National AIDS Programme, Ministry of Health; 2010.
14. Rapid situation assessments of HIV prevalence and risk factors among people injecting drugs in four cities of the Punjab. Islamabad: Nai Zindagi and Punjab Provincial AIDS Control Program; 2009 (http://www.aidsdatahub.org/sites/default/files/documents/Rapid_Situation_Assessments.pdf, accessed 8 July 2019).
15. Mirzoyan L, Berendes S, Jeffery C, Thomson J, Ben Othman H, Danon L, et al. New evidence on the HIV epidemic in Libya: why countries must implement prevention programs among people who inject drugs. *J Acquir Immune Defic Syndr*. 2013 Apr 15;62(5):577–83. doi.org/10.1097/QAI.0b013e318284714a PMID:23337363.
16. Afsar Kazerooni P, Amini Lari M, Joolaei H, Parsa N. Knowledge and attitude of male intravenous drug users on HIV/AIDS associated high risk behaviors in Shiraz Pir-Banon jail, Fars Province, Southern Iran. *Iran Red Crescent Med J*. 2010;12(3):334–6.
17. HIV Risk among Heroin and Injecting Drug Users in Muscat, Oman: quantitative survey, preliminary data. Muscat: Oman Ministry of Health; 2006.
18. Asadi S, Marjani M. Prevalence of intravenous drug use-associated infections. *Iranian Journal of Clinical Infectious Diseases*. 2006;1(2):59–62.
19. Todd CS, Nasir A, Stanekzai MR, Fiekert K, Rasuli MZ, Vlahov D, et al. Prevalence and correlates of HIV, syphilis, and hepatitis B and C infection and harm reduction program use among male injecting drug users in Kabul, Afghanistan: A cross-sectional assessment. *Harm Reduct J*. 2011 Aug 25;8(1):22. doi.org/10.1186/1477-7517-8-22 PMID:21867518.
20. Razzaghi EM, Movaghar AR, Green TC, Khoshnood K. Profiles of risk: a qualitative study of injecting drug users in Tehran, Iran. *Harm Reduct J*. 2006 Mar 18;3(1):12. doi.org/10.1186/1477-7517-3-12 PMID:16545137.
21. An integrated bio-behavioral surveillance study among four vulnerable groups in Lebanon: men who have sex with men; prisoners; commercial sex workers and intravenous drug users. Mid-term report. Beirut: Mishwar IBBS_Lebanon; 2008.
22. Assessment of HIV risk and seroprevalence among drug users in greater Damascus. Damascus: Syrian Ministry of Health, United Nations Office on Drugs and Crime and the Joint United Nations Programme on HIV/AIDS; 2008.



23. Emmanuel F, Fatima M. Coverage to curb the emerging HIV epidemic among injecting drug users in Pakistan: delivering prevention services where most needed. *Int J Drug Policy*. 2008 Apr;19 Suppl 1:S59–64. doi.org/10.1016/j.drugpo.2007.12.012 PMID:18281206.
24. HIV second generation surveillance in Pakistan. National report round III. Islamabad: National AIDS Control Program; 2008 (www.nacp.gov.pk/library/reports/Surveillance%20&%20Research/HIV-AIDS%20Surveillance%20Project-HASP/HIV%20Second%20Generation%20Surveillance%20in%20Pakistan%20-%20National%20report%20Round%20III%202008.pdf, accessed 8 July 2019).
25. Sy T, Jamal MM. Epidemiology of hepatitis C virus (HCV) infection. *Int J Med Sci*. 2006;3(2):41–6. doi.org/10.7150/ijms.3.41 PMID:16614741.
26. Integrated behavioral & biological surveillance (IBBS) in selected cities of Afghanistan: Findings of the 2012 IBBS survey and comparison to 2009 IBBS survey. Kabul: National AIDS Control Programme, Ministry of Public Health; 2012 (<http://www.nacp-moph.gov.af/wp-content/uploads/2015/08/IBBS-2nd-Round-Final-Report.pdf>, accessed 8 July 2019).
27. Saleh E, Mcfarland W, Rutherford G, Mandel J, El-Shazaly M, Coates T. Sentinel surveillance for HIV and high risk behaviors among injection drug users in Alexandria, Egypt. Abstract no. 13124, presented at the XII International AIDS Conference. Geneva, Switzerland, 28 June–3 July 1998.
28. Mohtasham Amiri Z, Rezvani M, Jafari Shakib R, Jafari Shakib A. Prevalence of hepatitis C virus infection and risk factors of drug using prisoners in Guilan province. *East Mediterr Health J*. 2007 Mar-Apr;13(2):250–6. PMID:17684845.
29. Mir-Nasseri MM, Mohammadkhani A, Tavakkoli H, Ansari E, Poustchi H. Incarceration is a major risk factor for blood-borne infection among intravenous drug users: Incarceration and blood borne infection among intravenous drug users. *Hepat Mon*. 2011 Jan;11(1):19–22. PMID:22087111.
30. Behnaz K, et al. Prevalence and risk factors of HIV, hepatitis B virus and hepatitis C virus infections in drug addicts among Gorgan prisoners. *J Med Sci*. 2007;7(2):252–4. doi.org/10.3923/jms.2007.252.254.
31. Altaf A, Shah SA, Zaidi NA, Memon A, Nadeem-ur-Rehman, Wray N. High risk behaviors of injection drug users registered with harm reduction programme in Karachi, Pakistan. *Harm Reduct J*. 2007 Feb 10;4(1):7. doi.org/10.1186/1477-7517-4-7 PMID:17291354.
32. Njoh J, Zimmo S. Prevalence of antibodies to hepatitis C virus in drug-dependent patients in Jeddah, Saudi Arabia. *East Afr Med J*. 1997 Feb;74(2):89–91. PMID:9185392.
33. Lansky A, Finlayson T, Johnson C, Holtzman D, Wejnert C, Mitsch A, et al. Estimating the number of persons who inject drugs in the united states by meta-analysis to calculate national rates of HIV and hepatitis C virus infections. *PLoS One*. 2014 May 19;9(5):e97596. doi.org/10.1371/journal.pone.0097596 PMID:24840662.
34. Razzaghi E, Nassirimanesh B, Afshar P, Ohiri K, Claeson M, Power R. HIV/AIDS harm reduction in Iran. *Lancet*. 2006 Aug 5;368(9534):434–5. doi.org/10.1016/S0140-6736(06)69132-0 PMID:16890814.
35. Butler D. Libya progresses on HIV. *Nature*. 2008 Mar 13;452(7184):138. doi.org/10.1038/452138c PMID:18337782.
36. Aceijas C, Rhodes T. Global estimates of prevalence of HCV infection among injecting drug users. *Int J Drug Policy*. 2007 Oct;18(5):352–8. doi.org/10.1016/j.drugpo.2007.04.004 PMID:17854722.



5. HCV epidemiology among populations at intermediate risk of exposure to HCV

1. Naing C, Mak JW, Ahmed SI, Maung M. Relationship between hepatitis C virus infection and type 2 diabetes mellitus: meta-analysis. *World J Gastroenterol*. 2012 Apr 14;18(14):1642–51. <http://dx.doi.org/10.3748/wjg.v18.i14.1642> PMID:22529694.
2. Everhart J. A confluence of epidemics: does hepatitis C cause type 2 diabetes? *Hepatology*. 2001 Mar;33(3):762–3. <http://dx.doi.org/10.1002/hep.510330336> PMID:11230760.
3. Abdelwahab SF, Hashem M, Galal I, Sobhy M, Abdel-Ghaffar TS, Galal G, et al. Incidence of hepatitis C virus infection among Egyptian healthcare workers at high risk of infection. *J Clin Virol*. 2013 May;57(1):24–8. <http://dx.doi.org/10.1016/j.jcv.2013.01.005> PMID:23375237.
4. Munier A, Marzouk D, Abravanel F, El-Daly M, Taylor S, Mamdouh R, et al. Frequent transient hepatitis C viremia without seroconversion among healthcare workers in Cairo, Egypt. *PLoS One*. 2013;8(2):e57835. <http://dx.doi.org/10.1371/journal.pone.0057835> PMID:23469082.
5. Okasha O, Munier A, Delarocque-Astagneau E, El Houssinie M, Rafik M, Bassim H, et al. Hepatitis C virus infection and risk factors in health-care workers at Ain Shams University Hospitals, Cairo, Egypt. *East Mediterr Health J*. 2015 May 19;21(3):199–212. PMID:26074220.
6. Saleh DA, Shebl FM, El-Kamary SS, Magder LS, Allam A, Abdel-Hamid M, et al. Incidence and risk factors for community-acquired hepatitis C infection from birth to 5 years of age in rural Egyptian children. *Trans R Soc Trop Med Hyg*. 2010 May;104(5):357–63. <http://dx.doi.org/10.1016/j.trstmh.2010.01.009> PMID:20153495.
7. Heijnen M, Mumtaz GR, Abu-Raddad LJ. Status of HIV and hepatitis C virus infections among prisoners in the Middle East and North Africa: review and synthesis. *J Int AIDS Soc*. 2016 May 27;19(1):20873. <http://dx.doi.org/10.7448/IAS.19.1.20873> PMID:27237131.
8. Kleven RM, Hu DJ, Jiles R, Holmberg SD. Evolving epidemiology of hepatitis C virus in the United States. *Clin Infect Dis*. 2012 Jul;55 Suppl 1:S3–9. <http://dx.doi.org/10.1093/cid/cis393> PMID:22715211.
9. Wong J, Moore D, Kanter S, Buxton J, Robert W, Gustafson R, et al.; ManCount Study Team. Seroprevalence of hepatitis C and correlates of seropositivity among men who have sex with men in Vancouver, Canada: a cross-sectional survey. *Sex Transm Infect*. 2015 Sep;91(6):430–3. <http://dx.doi.org/10.1136/sextrans-2014-051928> PMID:25872512.
10. Abu-Raddad LJ, Akala FA, Semini I, Riedner G, Wilson D, Tawil O. Characterizing the HIV/AIDS epidemic in the Middle East and North Africa: time for strategic action. Washington, DC: World Bank; 2010.

6. HCV epidemiology among the general population

1. Mostafa A, Taylor SM, el-Daly M, el-Hoseiny M, Bakr I, Arafa N, et al. Is the hepatitis C virus epidemic over in Egypt? Incidence and risk factors of new hepatitis C virus infections. *Liver Int*. 2010 Apr;30(4):560–6. <http://dx.doi.org/10.1111/j.1478-3231.2009.02204.x> PMID:20141592.
2. Mohamed MK, Abdel-Hamid M, Mikhail NN, Abdel-Aziz F, Medhat A, Magder LS, et al. Intrafamilial transmission of hepatitis C in Egypt. *Hepatology*. 2005 Sep;42(3):683–7. <http://dx.doi.org/10.1002/hep.20811> PMID:16032698.



3. Saleh DA, Shebl F, Abdel-Hamid M, Narooz S, Mikhail N, El-Batanony M, et al. Incidence and risk factors for hepatitis C infection in a cohort of women in rural Egypt. *Trans R Soc Trop Med Hyg.* 2008 Sep;102(9):921–8. <http://dx.doi.org/10.1016/j.trstmh.2008.04.011> PMID:18514243.
4. Miller FD, Abu-Raddad LJ. Evidence of intense ongoing endemic transmission of hepatitis C virus in Egypt. *Proc Natl Acad Sci USA.* 2010 Aug 17;107(33):14757–62. <http://dx.doi.org/10.1073/pnas.1008877107> PMID:20696911.
5. Mohamoud YA, Mumtaz GR, Riome S, Miller D, Abu-Raddad LJ. The epidemiology of hepatitis C virus in Egypt: a systematic review and data synthesis. *BMC Infect Dis.* 2013 Jun 24;13(1):288. <http://dx.doi.org/10.1186/1471-2334-13-288> PMID:23799878.
6. Al-Ani MH, Rasul TH. Hepatitis B and C viral infections in children with acute leukemia in Erbil city. *J Arab Board of Health Specializations.* 2011;12(1):21–9.
7. El-Zanaty F, Way A. Egypt demographic and health survey 2008. Cairo: Ministry of Health and Population, El-Zanaty and Associates, and Macro International; 2009.
8. Ministry of Health and Population, Egypt, El-Zanaty and Associates, and ICF International, Egypt health issues survey 2015. Cairo and Rockville, Maryland: Ministry of Health and Population and ICF International; 2015.
9. Cuadros DF, Branscum AJ, Miller FD, Abu-Raddad LJ. Spatial epidemiology of hepatitis C virus infection in Egypt: analyses and implications. *Hepatology.* 2014 Oct;60(4):1150–9. <http://dx.doi.org/10.1002/hep.27248> PMID:24913187.
10. Qureshi H, Bile KM, Jooma R, Alam SE, Afridi HU. Prevalence of hepatitis B and C viral infections in Pakistan: findings of a national survey appealing for effective prevention and control measures. *East Mediterr Health J.* 2010;16 Suppl:S15–23. PMID:21495584.
11. Umer M, Iqbal M. Hepatitis C virus prevalence and genotype distribution in Pakistan: Comprehensive review of recent data. *World J Gastroenterol.* 2016 Jan 28;22(4):1684–700. <http://dx.doi.org/10.3748/wjg.v22.i4.1684> PMID:26819533.
12. Umar M, Bushra HT, Ahmad M, Data A, Ahmad M, Khurram M, et al. Hepatitis C in Pakistan: a review of available data. *Hepat Mon.* 2010 Summer;10(3):205–14. PMID:22308140.
13. Mohd Hanafiah K, Groeger J, Flaxman AD, Wiersma ST. Global epidemiology of hepatitis C virus infection: new estimates of age-specific antibody to HCV seroprevalence. *Hepatology.* 2013 Apr;57(4):1333–42. <http://dx.doi.org/10.1002/hep.26141> PMID:23172780.
14. Lavanchy D. Evolving epidemiology of hepatitis C virus. *Clin Microbiol Infect.* 2011 Feb;17(2):107–15. <http://dx.doi.org/10.1111/j.1469-0691.2010.03432.x> PMID:21091831.
15. Cornberg M, Razavi HA, Alberti A, Bernasconi E, Buti M, Cooper C, et al. A systematic review of hepatitis C virus epidemiology in Europe, Canada and Israel. *Liver Int.* 2011 Jul;31 Suppl 2:30–60. <http://dx.doi.org/10.1111/j.1478-3231.2011.02539.x> PMID:21651702.



7. Modes of exposure to HCV infection in the WHO Eastern Mediterranean Region

1. Frank C, Mohamed MK, Strickland GT, Lavanchy D, Arthur RR, Magder LS, et al. The role of parenteral antischistosomal therapy in the spread of hepatitis C virus in Egypt. *Lancet*. 2000 Mar 11;355(9207):887–91. 10.1016/S0140-6736(99)06527-7 PMID:10752705.
2. Strickland GT. Liver disease in Egypt: hepatitis C superseded schistosomiasis as a result of iatrogenic and biological factors. *Hepatology*. 2006 May;43(5):915–22. 10.1002/hep.21173 PMID:16628669.
3. El-Zanaty F, Way A. Egypt demographic and health survey 2008. Cairo, Egypt: Ministry of Health, El-Zanaty and Associates, and Macro International; 2009.
4. Ministry of Health and Population Egypt, El-Zanaty and Associates Egypt and ICF International. Egypt Health issues survey 2015. Cairo, and Rockville (MD): Ministry of Health and Population and ICF International; 2015.
5. Mohamoud YA, Mumtaz GR, Riome S, Miller D, Abu-Raddad LJ. The epidemiology of hepatitis C virus in Egypt: a systematic review and data synthesis. *BMC Infect Dis*. 2013 Jun 24;13(1):288. 10.1186/1471-2334-13-288 PMID:23799878.
6. Visco-Comandini U, Cappiello G, Liuzzi G, Tozzi V, Anzidei G, Abbate I, et al.; Libya Project Task Force. Monophyletic HIV type 1 CRF02-AG in a nosocomial outbreak in Benghazi, Libya. *AIDS Res Hum Retroviruses*. 2002 Jul 1;18(10):727–32. 10.1089/088922202760072366 PMID:12167281.
7. de Oliveira T, Pybus OG, Rambaut A, Salemi M, Cassol S, Ciccozzi M, et al.; Benghazi Study Group. Molecular epidemiology: HIV-1 and HCV sequences from Libyan outbreak. *Nature*. 2006 Dec 14;444(7121):836–7. 10.1038/444836a PMID:17171825.
8. Yerly S, Quadri R, Negro F, Barbe KP, Cheseaux JJ, Burgisser P, et al. Nosocomial outbreak of multiple bloodborne viral infections. *J Infect Dis*. 2001 Aug 1;184(3):369–72. 10.1086/322036 PMID:11443566.
9. Hassan NF, el Ghorab NM, Abdel Rehim MS, el Sharkawy MS, el Sayed NM, Emara K, et al. HIV infection in renal dialysis patients in Egypt. *AIDS*. 1994 Jun;8(6):853. 10.1097/00002030-199406000-00023 PMID:8086148.
10. El Sayed NM, Gomatos PJ, Beck-Sagué CM, Dietrich U, von Briesen H, Osmanov S, et al. Epidemic transmission of human immunodeficiency virus in renal dialysis centers in Egypt. *J Infect Dis*. 2000 Jan;181(1):91–7. 10.1086/315167 PMID:10608755.
11. Hauri AM, Armstrong GL, Hutin YJ. The global burden of disease attributable to contaminated injections given in health care settings. *Int J STD AIDS*. 2004 Jan;15(1):7–16. 10.1258/095646204322637182 PMID:14769164.
12. Pépin J, Abou Chakra CN, Pépin E, Nault V, Valiquette L. Evolution of the global burden of viral infections from unsafe medical injections, 2000–2010. *PLoS One*. 2014 Jun 9;9(6):e99677. 10.1371/journal.pone.0099677 PMID:24911341.
13. Altaf A, Fatmi Z, Ajmal A, Hussain T, Qahir H, Agboatwalla M. Determinants of therapeutic injection overuse among communities in Sindh, Pakistan. *J Ayub Med Coll Abbottabad*. 2004 Jul-Sep;16(3):35–8. PMID:15631369.
14. Janjua NZ, Hutin YJ, Akhtar S, Ahmad K. Population beliefs about the efficacy of injections in Pakistan's Sindh province. *Public Health*. 2006 Sep;120(9):824–33. 10.1016/j.puhe.2006.05.004 PMID:16876212.



15. Mujeeb SA. Blood transfusion—a potential source of HIV/AIDS spread. *J Pak Med Assoc.* 1993 Jan;43(1):1. PMID:8474211.
16. Mirmomen S, Alavian SM, Hajarizadeh B, Kafaee J, Yektaparast B, Zahedi MJ, et al. Epidemiology of hepatitis B, hepatitis C, and human immunodeficiency virus infections in patients with beta-thalassemia in Iran: a multicenter study. *Arch Iran Med.* 2006 Oct;9(4):319–23. PMID:17061602.
17. Alavian SM, Bagheri-Lankarani K, Mahdavi-Mazdeh M, Nourozi S. Hepatitis B and C in dialysis units in Iran: changing the epidemiology. *Hemodial Int.* 2008 Jul;12(3):378–82. 10.1111/j.1542-4758.2008.00284.x PMID: 18638096.
18. Mohamoud YA, Miller FD, Abu-Raddad LJ. Potential for human immunodeficiency virus parenteral transmission in the Middle East and North Africa: an analysis using hepatitis C virus as a proxy biomarker. *World J Gastroenterol.* 2014 Sep 28;20(36):12734–52. 10.3748/wjg.v20.i36.12734 PMID:25278675.
19. Progress report on HIV/AIDS and 3 by 5 initiative. Cairo: WHO Regional Office for the Eastern Mediterranean; July 2005 (EM/RC52/INF.DOC.1).
20. Khawaja ZA, Gibney L, Ahmed AJ, Vermund SH. HIV/AIDS and its risk factors in Pakistan. *AIDS.* 1997 Jun;11(7):843–8. 10.1097/00002030-199707000-00002 PMID:9189208.
21. HIV/AIDS in Pakistan. Washington (DC): World Bank; 2005.
22. HIV/AIDS in Afghanistan. Washington (DC): World Bank; 2006.
23. Cheraghali AM. Blood safety concerns in the Eastern Mediterranean region. *Hepat Mon.* 2011;11(6):422–42. PMID:22087172.
24. Progress towards universal access to HIV prevention, treatment and care in the health sector. Report on a baseline survey for the year 2005 in the WHO Eastern Mediterranean Region. Draft. WHO Regional Office for the Eastern Mediterranean; 2006 (unpublished report).
25. Luby S, Khanani R, Zia M, Vellani Z, Ali M, Qureshi AH, et al. Evaluation of blood bank practices in Karachi, Pakistan, and the government's response. *Health Policy Plan.* 2000 Jun;15(2):217–22. 10.1093/heapol/15.2.217 PMID:10837045.
26. Zafar A, Aslam N, Nasir N, Meraj R, Mehraj V. Knowledge, attitudes and practices of health care workers regarding needle stick injuries at a tertiary care hospital in Pakistan. *J Pak Med Assoc.* 2008 Feb;58(2):57–60. PMID:18333520.
27. Kabbash IA, El-Sayed NM, Al-Nawawy AN, Abou Salem Mel-S, El-Deek B, Hassan NM. Risk perception and precautions taken by health care workers for HIV infection in haemodialysis units in Egypt. *East Mediterr Health J.* 2007 Mar-Apr;13(2):392–407. PMID:17684860.
28. Talaat M, Kandeel A, Rasslan O, Hajjeh R, Hallaj Z, El-Sayed N, et al. Evolution of infection control in Egypt: achievements and challenges. *Am J Infect Control.* 2006 May;34(4):193–200. 10.1016/j.ajic.2005.05.028 PMID:16679176.
29. Laraqui O, Laraqui S, Tripodi D, Zahraoui M, Caubet A, Verger C, et al. Evaluation des connaissances, attitudes et pratiques sur les accidents d'exposition au sang en milieu de soins au Maroc [Assessing knowledge, attitude, and practice on occupational blood exposure in caregiving facilities, in Morocco]. *Med Mal Infect.* 2008 Dec;38(12):658–66. 10.1016/j.medmal.2008.09.009 PMID:18954949.
30. Askarian M, Mirzaei K, McLaws ML. Attitudes, beliefs, and infection control practices of Iranian dentists associated with HIV-positive patients. *Am J Infect Control.* 2006 Oct;34(8):530–3. 10.1016/j.ajic.2006.03.006 PMID:17015160.



31. Askarian M, Mirzaei K, Cookson B. Knowledge, attitudes, and practice of Iranian dentists with regard to HIV-related disease. *Infect Control Hosp Epidemiol*. 2007 Jan;28(1):83–7. 10.1086/509851 PMID:17230393.
32. Al-Jadiry MF. Viral hepatitis markers screen in children with acute lymphoblastic leukemia experience of Children Welfare Teaching Hospital. *J Fac Med Baghdad*. 2008;50(2):223–30.
33. Health emergency highlights. Emergency Risk Management and Humanitarian Response, 2014, issue 19 (http://www.who.int/hac/donorinfo/highlights/erm_highlights_issue19_october2014.pdf?ua=1, accessed 8 July 2019).
34. World Health Organization Regional Office for the Eastern Mediterranean. Regional Director, Annual Reports. Emergency preparedness and response. 2013 (<http://www.emro.who.int/annual-report/2013/emergency-preparedness-and-response.html>, accessed 8 July 2019).
35. World Health Organization. Conflict and humanitarian crisis in Iraq. Public health risk assessment and interventions. 24 October 2014 (http://who.int/hac/crises/irq/iraq_phra_24october2014.pdf, accessed 8 July 2019).
36. Chemaitelly H, Chaabna K, Abu-Raddad LJ. The Epidemiology of Hepatitis C Virus in the Fertile Crescent: Systematic Review and Meta-Analysis. *PLoS One*. 2015 Aug 21;10(8):e0135281. 10.1371/journal.pone.0135281 PMID:26296200.
37. Janjua NZ. Injection practices and sharp waste disposal by general practitioners of Murree, Pakistan. *J Pak Med Assoc*. 2003 Mar;53(3):107–11. PMID:12779025.
38. Janjua NZ, Akhtar S, Hutin YJ. Injection use in two districts of Pakistan: implications for disease prevention. *Int J Qual Health Care*. 2005 Oct;17(5):401–8. 10.1093/intqhc/mzi048 PMID:15883127.
39. Todd CS, Barbera-Lainez Y, Doocy SC, Ahmadzai A, Delawar FM, Burnham GM. Prevalence of human immunodeficiency virus infection, risk behavior, and HIV knowledge among tuberculosis patients in Afghanistan. *Sex Transm Dis*. 2007 Nov;34(11):878–82. 10.1097/OLQ.0b013e318095068a PMID:17595595.
40. Zali M-R, Aghazadeh R, Nowroozi A, Amir-Rasouly H. Anti-HCV antibody among Iranian IV drug users: is it a serious problem. *Arch Iran Med*. 2001;4(3):115–9.
41. Hosseini Asl SK, Avijgan M, Mohamadnejad M. High prevalence of HBV, HCV, and HIV infections: in gypsy population residing in Shar-e-Kord. *Arch Iranian Med*, 2004. 7(1):22–4.
42. Alrajhi AA, Halim MA, Al-Abdely HM. Mode of transmission of HIV-1 in Saudi Arabia. *AIDS*. 2004 Jul 2;18(10):1478–80. 10.1097/01.aids.0000131344.91536.64 PMID:15199329.
43. Mansoor AB, Fungladda W, Kaewkungwal J, Wongwit W. Gender differences in KAP related to HIV/AIDS among freshmen in Afghan universities. *Southeast Asian J Trop Med Public Health*. 2008 May;39(3):404–18. PMID:18564679.
44. Sudan National HIV/AIDS Control Programme. HIV/AIDS/STIs prevalence, knowledge, attitude, practices and risk factors among university students and military personnel. Khartoum, Sudan: Federal Ministry of Health; 2004.
45. Zahraoui-Mehadji M, Baakrim MZ, Laraoui S, Laraoui O, El Kabouss Y, Verger C, et al. Risque infectieux lie au sang chez les coiffeurs-barbiers traditionnels et leurs clients au Maroc [Infectious risks associated with blood exposure for traditional barbers and their customers in Morocco]. *Sante*. 2004 Oct-Dec;14(4):211–6. PMID:15745870.
46. Janjua NZ, Nizamy MA. Knowledge and practices of barbers about hepatitis B and C transmission in Rawalpindi and Islamabad. *J Pak Med Assoc*. 2004 Mar;54(3):116–9. PMID:15129868.



47. Idrees M, Riazuddin S. Frequency distribution of hepatitis C virus genotypes in different geographical regions of Pakistan and their possible routes of transmission. *BMC Infect Dis.* 2008 May 23;8(1):69. 10.1186/1471-2334-8-69 PMID:18498666.
48. Okasha O, Munier A, Delarocque-Astagneau E, El Houssinie M, Rafik M, Bassim H, et al. Hepatitis C virus infection and risk factors in health-care workers at Ain Shams University Hospitals, Cairo, Egypt. *East Mediterr Health J.* 2015 May 19;21(3):199–212. PMID:26074220.
49. Derbala M, Chandra P, Amer A, John A, Sharma M, Amin A, et al. Re-examination of the relationship between the prevalence of hepatitis C virus and parenteral antischistosomal therapy among Egyptians resident in Qatar. *Clin Exp Gastroenterol.* 2014 Nov 3;7:427–33. 10.2147/CEG.S65369 PMID:25395869.
50. Edris A, Nour MO, Zedan OO, Mansour AE, Ghandour AA, Omran T. Seroprevalence and risk factors for hepatitis B and C virus infection in Damietta Governorate, Egypt. *East Mediterr Health J.* 2014 Oct 20;20(10):605–13. PMID:25356691.
51. Zuure FR, Bouman J, Martens M, Vanhommerig JW, Urbanus AT, Davidovich U, et al. Screening for hepatitis B and C in first-generation Egyptian migrants living in the Netherlands. *Liver Int.* 2013 May;33(5):727–38. 10.1111/liv.12131 PMID:23448397.
52. Mohamed MK, Bakr I, El-Hoseiny M, Arafa N, Hassan A, Ismail S, et al. HCV-related morbidity in a rural community of Egypt. *J Med Virol.* 2006 Sep;78(9):1185–9. 10.1002/jmv.20679 PMID:16847958.
53. Stoszek SK, Abdel-Hamid M, Narooz S, El Daly M, Saleh DA, Mikhail N, et al. Prevalence of and risk factors for hepatitis C in rural pregnant Egyptian women. *Trans R Soc Trop Med Hyg.* 2006 Feb;100(2):102–7. 10.1016/j.trstmh.2005.05.021 PMID:16289168.
54. Arafa N, El Hoseiny M, Rekacewicz C, Bakr I, El-Kafrawy S, El Daly M, et al. Changing pattern of hepatitis C virus spread in rural areas of Egypt. *J Hepatol.* 2005 Sep;43(3):418–24. 10.1016/j.jhep.2005.03.021 PMID:16019104.
55. el-Sadawy M, Ragab H, el-Toukhy H, el-Mor Ael-L, Mangoud AM, Eissa MH, et al. Hepatitis C virus infection at Sharkia Governorate, Egypt: seroprevalence and associated risk factors. *J Egypt Soc Parasitol.* 2004 Apr;34(1) Suppl:367–84. PMID:15124747.
56. Strickland GT, Elhefni H, Salman T, Waked I, Abdel-Hamid M, Mikhail NN, et al. Role of hepatitis C infection in chronic liver disease in Egypt. *Am J Trop Med Hyg.* 2002 Oct;67(4):436–42. 10.4269/ajtmh.2002.67.436 PMID:12452500.
57. Abdel-Aziz F, Habib M, Mohamed MK, Abdel-Hamid M, Gamil F, Madkour S, et al. Hepatitis C virus (HCV) infection in a community in the Nile Delta: population description and HCV prevalence. *Hepatology.* 2000 Jul;32(1):111–5. 10.1053/jhep.2000.8438 PMID:10869297.
58. Nafeh MA, Medhat A, Shehata M, Mikhail NN, Swiffee Y, Abdel-Hamid M, et al. Hepatitis C in a community in Upper Egypt: I. Cross-sectional survey. *Am J Trop Med Hyg.* 2000 Nov-Dec;63(5-6):236–41. 10.4269/ajtmh.2000.63.236 PMID:11421370.
59. Angelico M, Renganathan E, Gandin C, Fathy M, Profili MC, Refai W, et al. Chronic liver disease in the Alexandria governorate, Egypt: contribution of schistosomiasis and hepatitis virus infections. *J Hepatol.* 1997 Feb;26(2):236–43. 10.1016/S0168-8278(97)80036-0 PMID:9059941.
60. El-Sayed HF, Abaza SM, Mehanna S, Winch PJ. The prevalence of hepatitis B and C infections among immigrants to a newly reclaimed area endemic for *Schistosoma mansoni* in Sinai, Egypt. *Acta Trop.* 1997 Nov;68(2):229–37. 10.1016/S0001-706X(97)00097-1 PMID:9386797.



61. El-Zayadi A, Khalifa AA, El-Misiery A, Naser AM, Dabbous H, Aboul-Ezz AA. Evaluation of risk factors for intrafamilial transmission of HCV infection in Egypt. *J Egypt Public Health Assoc.* 1997;72(1-2):33–51. PMID:17265624.
62. Mohamed MK, Hussein MH, Massoud AA, Rakhaa MM, Shoeir S, Aoun AA, et al. Study of the risk factors for viral hepatitis C infection among Egyptians applying for work abroad. *J Egypt Public Health Assoc.* 1996;71(1-2):113–47. PMID:17217004.
63. Quinti I, Renganathan E, El Ghazzawi E, Divizia M, Sawaf G, Awad S, et al. Seroprevalence of HIV and HCV infections in Alexandria, Egypt. *Zentralbl Bakteriol.* 1995 Dec;283(2):239–44. 10.1016/S0934-8840(11)80205-7 PMID:8825115.
64. International Conference on Schistosomiasis. Cairo, 14–18 February 1993. Hepatitis B, hepatitis C and schistosomiasis. *Med Chir Dig.* 1993;22(7):441–2.
65. Zakaria S, Al-Boraey Y. A community-based study of viral hepatitis infection in Giza Governorate, Egypt: Seroprevalence, risk factors and associated morbidity. *Med J Cairo Univ.* 2005;73(4):899–912.
66. Ramzi ZS, Abdulla AA, Al-Hadithi T, Al-Tawil N. Prevalence and risk factors for hepatitis C virus infection in hemodialysis patients in Sulaimani. *Zanco J Med Sci.* 2010;14(1):44–50.
67. Elzouki AN, Bushala M, Tobji RS, Khfaifi M. Prevalence of anti-hepatitis C virus antibodies and hepatitis C virus viraemia in chronic haemodialysis patients in Libya. *Nephrol Dial Transplant.* 1995;10(4):475–6. 10.1093/ndt/10.4.475 PMID:7542751.
68. Amar Y, Benamar L, Laouad I, Ezaïtouni F, Ouzeddoun N, Balafrej L. L'hépatite virale C dans un centre d'hémodialyse marocain: prévalence et facteurs de risque [Hepatitis C virus infection in a Moroccan haemodialysis unit: prevalence and risk factors]. *Gastroenterol Clin Biol.* 2005 Jun-Jul;29(6-7):746–7. 10.1016/S0399-8320(05)88202-8 PMID:16149187.
69. Sassi F, Gorgi Y, Ayed K, Abdallah TB, Lamouchi A, Maiz HB. Hepatitis C virus antibodies in dialysis patients in Tunisia: a single center study. *Saudi J Kidney Dis Transpl.* 2000 Apr-Jun;11(2):218–22. PMID:18209319.
70. al-Dhahry SHS, Aghanashinikar PN, al-Hasani MK, Buhl MR, Daar AS. Antibodies to hepatitis C virus in Omani patients with renal disease. *Transplant Proc.* 1992 Oct;24(5):1938–9. PMID:1384203.
71. Abboud O, Rashid A, Al-Kaabi S. Hepatitis C virus infection in hemodialysis patients in qatar. *Saudi J Kidney Dis Transpl.* 1995 Apr-Jun;6(2):151–3. PMID:18583855.
72. Kapoor M, el-Reshaïd K, al-Mufti S, Sanad NA, Koshy A. Is dialysis environment more important than blood transfusion in transmission of hepatitis C virus during hemodialysis? *Vox Sang.* 1993;65(4):331. 10.1111/j.1423-0410.1993.tb02176.x PMID:7508661.
73. Ayoola EA, Huraib S, Arif M, al-Faleh FZ, al-Rashed R, Ramia S, et al. Prevalence and significance of antibodies to hepatitis C virus among Saudi haemodialysis patients. *J Med Virol.* 1991 Nov;35(3):155–9. 10.1002/jmv.1890350303 PMID:1725179.
74. Al Nasser MN, al Mugeiren MA, Assuhaimi SA, Obineche E, Onwabalili J, Ramia S. Seropositivity to hepatitis C virus in Saudi haemodialysis patients. *Vox Sang.* 1992;62(2):94–7. 10.1111/j.1423-0410.1992.tb01177.x PMID:1325714.
75. Mitwalli A, al-Mohaya S, Al Wakeel J, El Gamal H, Rotimi V, Al-Zeben A, et al. Hepatitis C in chronic renal failure patients. *Am J Nephrol.* 1992;12(5):288–91. 10.1159/000168462 PMID:1336933.



76. Huraib S, Al-Rashed R, Aldrees A, Aljefry M, Arif M, Al-Faleh FA. High prevalence of and risk factors for hepatitis C in haemodialysis patients in Saudi Arabia: a need for new dialysis strategies. *Nephrol Dial Transplant*. 1995;10(4):470–4. 10.1093/ndt/10.4.470 PMID:7623989.
77. Bernieh B, Allam M, Halepota A, Mohamed AO, Parkar J, Tabbakh A. Prevalence of hepatitis C virus antibodies in hemodialysis patients in madinah Al munawarah. *Saudi J Kidney Dis Transpl*. 1995 Apr-Jun;6(2):132–5. PMID:18583851.
78. Al-Ghamdi SM, Al-Harbi AS. Hepatitis C Virus Sero-status in Hemodialysis Patients Returning from Holiday: Another Risk Factor for HCV Transmission. *Saudi J Kidney Dis Transpl*. 2001 Jan-Mar;12(1):14–20. PMID:18209355.
79. Kashem A, Karim MR. Prevalence of Hepatitis B and C among Hemodialysis Patients in Najran of Saudi Arabia. *Bangladesh Renal J*. 2002;21(2):34–8.
80. Kashem A, Nusairat I, Mohamad M, Ramzy M, Nemma J, Karim MR, et al. Hepatitis C virus among hemodialysis patients in Najran: prevalence is more among multi-center visitors. *Saudi J Kidney Dis Transpl*. 2003 Apr-Jun;14(2):206–11. PMID:18209450.
81. Hussein MM, Mooij JM, Hegazy MS, Bamaga MS. The impact of polymerase chain reaction assays for the detection of hepatitis C virus infection in a hemodialysis unit. *Saudi J Kidney Dis Transpl*. 2007 Mar;18(1):107–13. PMID: 17237902.
82. Al-Jiffri AM, Fadag RB, Ghabrah TM, Ibrahim A. Hepatitis C virus infection among patients on hemodialysis in jeddah: a single center experience. *Saudi J Kidney Dis Transpl*. 2003 Jan-Mar;14(1):84–9. PMID:17657097.
83. Gasim GI, Hamdan HZ, Hamdan SZ, Adam I. Epidemiology of hepatitis B and hepatitis C virus infections among hemodialysis patients in Khartoum, Sudan. *J Med Virol*. 2012 Jan;84(1):52–5. 10.1002/jmv.22256 PMID:22052648.
84. Baddoura R, Haddad C, Germanos M. Hepatitis B and C seroprevalence in the Lebanese population. *East Mediterr Health J*. 2002 Jan;8(1):150–6. PMID:15330570.
85. Zahran AM. Prevalence of seroconversion of hepatitis C virus among hemodialysis patients in Menoufia Governorate, Egypt. *Arab J Nephrol Transplant*. 2014 May;7(2):133–5. PMID:25366511.
86. Soliman AR, Momtaz Abd Elaziz M, El Lawindi MI. Evaluation of an isolation program of hepatitis C virus infected hemodialysis patients in some hemodialysis centers in egypt. *ISRN Nephrol*. 2012 Oct 31;2013:395467. PMID:24967226.
87. Sabry A. Proteinuria among renal transplant patients and its relation to hepatitis C virus and graft outcome: a single center experience. *Exp Clin Transplant*. 2010 Jun;8(2):91–7. PMID:20565364.
88. Gohar SA, Khalil RY, Elaish NM, Khedr EM, Ahmed MS. Prevalence of antibodies to hepatitis C virus in hemodialysis patients and renal transplant recipients. *J Egypt Public Health Assoc*. 1995;70(5-6):465–84. PMID:17214170.
89. Abdel-Wahab MF, Zakaria S, Kamel M, Abdel-Khaliq MK, Mabrouk MA, Salama H, et al. High seroprevalence of hepatitis C infection among risk groups in Egypt. *Am J Trop Med Hyg*. 1994 Nov;51(5):563–7. 10.4269/ajtmh.1994.51.563 PMID:7527186.
90. Goher SA, Abdel Ghany MM, Shaarawy AB, Sobhy SA. Dialyser reuse and hepatitis C virus in hemodialysis population in Egypt. *Sci Med J*. 1998;10(3):43–54.
91. Saddik Y, El Azoni M. Hepatitis C virus (HCV) antibodies in patients with chronic renal failure and treated with regular hemodialysis and those treated with renal transplantation. *Sci Med J*. 1997;9(3):79–99.



92. Samimi-Rad K, Hosseini M. Hepatitis C virus infection and HCV genotypes of hemodialysis patients. *Iran J Public Health*. 2008;37(3):146–52.
93. Othman B, Monem F. Prevalence of antibodies to hepatitis C virus among hemodialysis patients in Damascus, Syria. *Infection*. 2001 Oct;29(5):262–5. 10.1007/s15010-001-9156-7 PMID:11688903.
94. Ismail ZA. Prevalence of hepatitis C virus antibodies in hemodialysis patients. *Med J Cairo Univ*. 1994;62(2):283–91.
95. Khaleel HA, Turky AM, Al-Naaimi AM, Jalil RW, Mekhleef OA, Kareem SA, et al., Prevalence of HBsAg and anti HCV Ab among patients with suspected acute viral hepatitis in Baghdad, Iraq in 2010. *Epidemiology Reports*. 2014;1(1). 10.7243/2054-9911-1-1.
96. Al-Mahroos FT, Ebrahim A. Prevalence of hepatitis B, hepatitis C and human immune deficiency virus markers among patients with hereditary haemolytic anaemias. *Ann Trop Paediatr*. 1995 Jun;15(2):121–8. 10.1080/02724936.1995.11747759 PMID:7677412.
97. Al-Fawaz I, Ramia S. Decline in hepatitis B infection in sickle cell anaemia and beta thalassaemia major. *Arch Dis Child*. 1993 Nov;69(5):594–6. 10.1136/ad.69.5.594 PMID:8257183.
98. Ayoola EA, al-Mofleh IA, al-Faleh FZ, al-Rashed R, Arif MA, Ramia S, et al. Prevalence of antibodies to hepatitis C virus among Saudi patients with chronic liver diseases. *Hepatogastroenterology*. 1992 Aug;39(4):337–9. PMID:1385286.
99. Al-Waleedi AA, Khader YS. Prevalence of hepatitis B and C infections and associated factors among blood donors in Aden City, Yemen. *East Mediterr Health J*. 2012 Jun;18(6):624–9. PMID:22888620.
100. Adly AA, Ebeid FS. Cultural preferences and limited public resources influence the spectrum of thalassemia in Egypt. *J Pediatr Hematol Oncol*. 2015 May;37(4):281–4. 10.1097/MPH.0000000000000327 PMID:25811748.
101. Salama KM, Ibrahim OM, Kaddah AM, Boseila S, Ismail LA, Hamid MM. Liver enzymes in children with beta-Thalassemia major: Correlation with iron overload and viral hepatitis. *Open Access Maced J Med Sci*. 2015 Jun 15;3(2):287–92. 10.3889/oamjms.2015.059 PMID:27275237.
102. Mansour AK, Aly RM, Abdelrazek SY, Elghannam DM, Abdelaziz SM, Shahine DA, et al. Prevalence of HBV and HCV infection among multi-transfused Egyptian thalassemic patients. *Hematol Oncol Stem Cell Ther*. 2012;5(1):54–9. 10.5144/1658-3876.2012.54 PMID:22446611.
103. Awadalla HI, Ragab MH, Nassar NA, Osman MA. Risk factors of hepatitis C infection among Egyptian blood donors. *Cent Eur J Public Health*. 2011 Dec;19(4):217–21. PMID:22432397.
104. Barakat SH, El-Bashir N. Hepatitis C virus infection among healthy Egyptian children: prevalence and risk factors. *J Viral Hepat*. 2011 Nov;18(11):779–84. 10.1111/j.1365-2893.2010.01381.x PMID:21992795.
105. AbdulQawi K, Youssef A, Metwally MA, Ragih I, AbdulHamid M, Shaheen A. Prospective study of prevalence and risk factors for hepatitis C in pregnant Egyptian women and its transmission to their infants. *Croat Med J*. 2010 Jun;51(3):219–28. 10.3325/cmj.2010.51.219 PMID:20564765.
106. Kalil KA, Farghally HS, Hassanein KM, Abd-Elsayed AA, Hassanein FE. Hepatitis C virus infection among paediatric patients attending University of Assiut Hospital, Egypt. *East Mediterr Health J*. 2010 Apr;16(4):356–61. PMID:20795415.
107. Talaat M, El-Sayed N, Kandeel A, Azab MA, Afifi S, Youssef FG, et al. Sentinel surveillance for patients with acute hepatitis in Egypt, 2001–04. *East Mediterr Health J*. 2010 Feb;16(2):134–40. PMID:20799563.



108. Sharaf-Eldeen S, Salama K, Eldemerdash S, Hassan HMS, Semesem M. Hepatitis B and C viruses in Egyptian children with malignancy. *J Med Sci.* 2007;7(6):1003–8. 10.3923/jms.2007.1003.1008.
109. Kassem AS, el-Nawawy AA, Massoud MN, el-Nazar SY, Sobhi EM. Prevalence of hepatitis C virus (HCV) infection and its vertical transmission in Egyptian pregnant women and their newborns. *J Trop Pediatr.* 2000 Aug;46(4):231–3. 10.1093/tropej/46.4.231 PMID:10996985.
110. Farghaly AG, Mansour GA, Mahdy NH, Yousri A. Hepatitis B and C virus infections among patients with gingivitis and adult periodontitis: seroprevalence and public health importance. *J Egypt Public Health Assoc.* 1998;73(5-6):707–35. PMID:17217032.
111. Darwish NM, Abbas MO, Hady SI, Mohammed TA. Study of the high prevalence of HCV in Egypt. *J Egypt Public Health Assoc.* 1995;70(3-4):397–414. PMID:17214166.
112. Khalifa AS, Mitchell BS, Watts DM, El-Samahy MH, El-Sayed MH, Hassan NF, et al. Prevalence of hepatitis C viral antibody in transfused and nontransfused Egyptian children. *Am J Trop Med Hyg.* 1993 Sep;49(3):316–21. 10.4269/ajtmh.1993.49.316 PMID:7690525.
113. Poustchi H, Esmaili S, Mohamadkhani A, Nikmahzar A, Pourshams A, Sepanlou SG, et al. The impact of illicit drug use on spontaneous hepatitis C clearance: experience from a large cohort population study. *PLoS One.* 2011;6(8):e23830. 10.1371/journal.pone.0023830 PMID:21887326.
114. Mansour-Ghanaei F, Fallah M, Jafarshad R, Joukar F, Pourtahmasbi A, Bahari-Moghaddam A, et al. Seroprevalence of hepatitis B and C among residents of Guilan Nursing Home. *Hepat Mon.* 2007;7(3):139–41.
115. Abedian S, Firoozi M, Malekzadeh R. Etiology of liver cirrhosis in Iran: Single centre experience in a large referral centre, 2000–2011. *J Gastroenterol Hepatol.* 2013;28:615.
116. Guerra J, Garenne M, Mohamed MK, Fontanet A. HCV burden of infection in Egypt: results from a nationwide survey. *J Viral Hepat.* 2012 Aug;19(8):560–7. 10.1111/j.1365-2893.2011.01576.x PMID:22762140.
117. Scott DA, Constantine NT, Callahan J, Burans JP, Olson JG, al-Fadeel M, et al. The epidemiology of hepatitis C virus antibody in Yemen. *Am J Trop Med Hyg.* 1992 Jan;46(1):63–8. 10.4269/ajtmh.1992.46.63 PMID:1311155.
118. Kutrani H, El-Gatit A, Shekhteryea A, El-Gitait Y, Sudani O, Akoub S. [Demographic factors influencing hepatitis B and C infection in Benghazi, Libyan Arab Jamahiriya]. *East Mediterr Health J.* 2007 Jan-Feb;13(1):85–97. PMID:17546910 [In Arabic].
119. Cacoub P, Ohayon V, Sekkat S, Dumont B, Sbati A, Lunel F, et al. Etude épidémiologique et virologique des infections par le virus de l'hépatite C au Maroc. [Epidemiologic and virologic study of hepatitis C virus infections in Morocco]. *Gastroenterol Clin Biol.* 2000 Feb;24(2):169–73. PMID:12687957.
120. El-Shanshory MR, Kabbash IA, Soliman HH, Nagy HM, Abdou SH. Prevalence of hepatitis C infection among children with thalassaemia major in Mid Delta, Egypt: a single centre study. *Trans R Soc Trop Med Hyg.* 2013 Apr;107(4):224–8. 10.1093/trstmh/trs024 PMID:23343507.
121. Hagag SA, Koura SK, Abdel Hameed MF. Seroprevalence of hepatitis C virus infection among the volunteer blood donors in Zagazig. *Zagazig Univ Med J.* 1998;4(7):199–209.
122. El-Sayed NM, Gomatos PJ, Rodier GR, Wierzbza TF, Darwish A, Khashaba S, et al. Seroprevalence survey of Egyptian tourism workers for hepatitis B virus, hepatitis C virus, human immunodeficiency virus, and *Treponema pallidum* infections: association of hepatitis C virus infections with specific regions of Egypt. *Am J Trop Med Hyg.* 1996 Aug;55(2):179–84. 10.4269/ajtmh.1996.55.179 PMID:8780457.



123. El-Bendary M, Esmat G, Neamatallah M, Kamel E, Besheer T, Elalfy H, et al. Epidemiological aspects of intrafamilial spread of HCV infection in Egyptian population a pilot study. *Open J Gastroenterol*, 2014, 4, 228-36.
124. Mohamed HI, Saad ZM, Abd-Elreheem EM, Abd-ElGhany WM, Mohamed MS, Abd Elnaeem EA, et al. Hepatitis C, hepatitis B and HIV infection among Egyptian prisoners: seroprevalence, risk factors and related chronic liver diseases. *J Infect Public Health*. 2013 Jun;6(3):186–95. 10.1016/j.jiph.2012.12.003 PMID:23668463.
125. El-Kamary SS, Hashem M, Saleh DA, Ehab M, Sharaf SA, El-Mougy F, et al. Reliability of risk-based screening for hepatitis C virus infection among pregnant women in Egypt. *J Infect*. 2015 May;70(5):512–9. 10.1016/j.jinf.2015.01.009 PMID:25623176.
126. Eassa S, Eissa M, Sharaf SM, Ibrahim MH, Hassanein OM. Prevalence of hepatitis C virus infection and evaluation of a health education program in el-ghar village in zagazig, egypt. *J Egypt Public Health Assoc*. 2007;82(5-6):379–404. PMID:18706295.
127. El-Ghitany EM, Abdel Wahab MM, Abd El-Wahab EW, Hassouna S, Farghaly AG. A comprehensive hepatitis C virus risk factors meta-analysis (1989-2013): do they differ in Egypt? *Liver Int*. 2015 Feb;35(2):489–501. 10.1111/liv.12617 PMID:24923487.
128. Abu-Raddad LJ, Akala FA, Semini I, Riedner G, Wilson D, Tawil O. Characterizing the HIV/AIDS epidemic in the Middle East and North Africa : time for strategic action. Washington (DC): World Bank; 2010.
129. Mohamed MK, Abdel-Hamid M, Mikhail NN, Abdel-Aziz F, Medhat A, Magder LS, et al. Intrafamilial transmission of hepatitis C in Egypt. *Hepatology*. 2005 Sep;42(3):683–7. 10.1002/hep.20811 PMID:16032698.
130. Benova L, Mohamoud YA, Calvert C, Abu-Raddad LJ. Vertical transmission of hepatitis C virus: systematic review and meta-analysis. *Clin Infect Dis*. 2014 Sep 15;59(6):765–73. 10.1093/cid/ciu447 PMID:24928290.
131. Kumar RM, Frossad PM, Hughes PF. Seroprevalence and mother-to-infant transmission of hepatitis C in asymptomatic Egyptian women. *Eur J Obstet Gynecol Reprod Biol*. 1997 Dec;75(2):177–82. 10.1016/S0301-2115(97)00130-9 PMID:9447371.
132. Shebl FM, El-Kamary SS, Saleh DA, Abdel-Hamid M, Mikhail N, Allam A, et al. Prospective cohort study of mother-to-infant infection and clearance of hepatitis C in rural Egyptian villages. *J Med Virol*. 2009 Jun;81(6):1024–31. 10.1002/jmv.21480 PMID:19382251.
133. Al-Kubaisy WA, Niazi A, Kubba K. Lack of mother-to-newborn transmission of hepatitis C virus in Iraqi women: a prospective study with hepatitis C virus RNA testing. *J Arab Board of Health Specializations*. 2000;2(2).
134. Aziz S, Hossain N, Karim SA, Rajper J, Soomro N, Noorulain W, et al. Vertical transmission of hepatitis C virus in low to middle socio-economic pregnant population of Karachi. *Hepatol Int*. 2011 Jun;5(2):677–80. 10.1007/s12072-010-9229-8 PMID:21484109.
135. Benova L, Awad SF, Miller FD, Abu-Raddad LJ. Estimation of hepatitis C virus infections resulting from vertical transmission in Egypt. *Hepatology*. 2015 Mar;61(3):834–42. 10.1002/hep.27596 PMID:25366418.



8. Analytical insights into HCV transmission dynamics in WHO's Eastern Mediterranean Region

1. Denniston MM, Jiles RB, Drobeniuc J, Klevens RM, Ward JW, McQuillan GM, et al. Chronic hepatitis C virus infection in the United States, National Health and Nutrition Examination Survey 2003 to 2010. *Ann Intern Med.* 2014 Mar 4;160(5):293–300. <http://dx.doi.org/10.7326/M13-1133> PMID:24737271.
2. Armstrong GL, Wasley A, Simard EP, McQuillan GM, Kuhnert WL, Alter MJ. The prevalence of hepatitis C virus infection in the United States, 1999 through 2002. *Ann Intern Med.* 2006 May 16;144(10):705–14. <http://dx.doi.org/10.7326/0003-4819-144-10-200605160-00004> PMID:16702586.
3. Lansky A, Finlayson T, Johnson C, Holtzman D, Wejnert C, Mitsch A, et al. Estimating the number of persons who inject drugs in the united states by meta-analysis to calculate national rates of HIV and hepatitis C virus infections. *PLoS One.* 2014 May 19;9(5):e97596. <http://dx.doi.org/10.1371/journal.pone.0097596> PMID:24840662.
4. Cuadros DF, Branscum AJ, Miller FD, Abu-Raddad LJ. Spatial epidemiology of hepatitis C virus infection in Egypt: analyses and implications. *Hepatology.* 2014 Oct;60(4):1150–9. <http://dx.doi.org/10.1002/hep.27248> PMID:24913187.
5. Prevalence of hepatitis B & C in Pakistan. Islamabad: Pakistan Medical Research Council; 2008.
6. Egypt health issues survey. Cairo: Ministry of Health and Population [Egypt], El-Zanaty and Associates [Egypt], ICF International; 2015.

9. Responding to viral hepatitis with a focus on HCV infection across WHO's Eastern Mediterranean Region: the way forward

1. Global report on access to hepatitis C treatment. Focus on overcoming barriers. Geneva: World Health Organization; 2016.
2. World Health Organization. Global health sector strategy on viral hepatitis, 2016–2021. Geneva: World Health Organization; 2015.
3. World Health Organization Regional Office for the Eastern Mediterranean. Regional action plan for the implementation of the Global Strategy for Viral Hepatitis 2017–2021. Cairo: Regional Office for the Eastern Mediterranean; 2016.

Epidemiology of hepatitis C virus in the WHO Eastern Mediterranean Region: implications for strategic action presents the results and findings of the Eastern Mediterranean Hepatitis C Virus Epidemiology Synthesis Project, which aimed to characterize the epidemiology of hepatitis C virus across countries through comprehensive systematic reviews and synthesis of published and unpublished epidemiological measures. In the Region, hepatitis C virus accounts for about two thirds of viral hepatitis morbidity and mortality. This report provides an analytical description of its epidemiology among the different populations at risk of acquiring the infection, discusses risk factors and major drivers of transmission, and estimates prevalence among the various populations at risk for each country of the Region.

