

## Human immunodeficiency virus and viral hepatitis among high-risk groups: Understanding the knowledge gap in the Middle East and North Africa Region

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**Author contributions:** Melhem NM designed and wrote the paper; Rahhal N, Charide R and Kreidieh K reviewed the literature, prepared the tables and contributed to the write-up; El-Khatib R critically read the manuscript.

**Conflict-of-interest statement:** The authors declare no conflict of interest.

**Data sharing statement:** This is not applicable to this review. The authors did not generate the data but rather relied on published ones.

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Received: June 24, 2015

Peer-review started: June 25, 2015

First decision: August 26, 2015

Revised: September 26, 2015

Accepted: October 23, 2015

Article in press: October 27, 2015

Published online: November 8, 2015

### Abstract

**AIM:** To identify gaps in the existing knowledge on single, dual and triple infections of human immunodeficiency virus (HIV), hepatitis B virus (HBV) and hepatitis C virus (HCV) in the Middle East and North Africa (MENA) region among men who have sex with men (MSMs), female sex workers (FSWs), injecting drug users (IDUs) and prisoners.

**METHODS:** We performed an extensive literature search on articles published on the topic in the 25 countries of the MENA region. PubMed database was used as the main search engine. Case reports, case series, qualitative studies, editorials, commentaries, authors' replies and animal studies were excluded. Original articles and reviews dealing with the prevalence of HIV, HBV and HCV and their co-infection were included. Data on population type, sample size, age and markers of infections were extracted from the relevant studies.

**RESULTS:** HIV, HBV and HCV are blood-borne viruses with similar modes of transmission. The categories of people at high risk of acquiring HIV-1, HBV and HCV commonly include: MSMs, FSW and IDUs. It is well established that HIV-positive individuals co-infected with HBV or HCV suffer from liver pathology associated with morbidity and mortality. Moreover, HIV-infected individuals do not respond well to treatment for HBV or HCV and hence are at increased risk of hepatic toxicity. Consequently, co-infection of HIV-positive individuals with HBV and/or HCV is a global health problem of

significant magnitude. Our review reveals the paucity of epidemiological data for key populations in many countries of the region. Limited number of studies exists in the MENA region on the status of HIV, HBV and HCV and their co-infections among prisoners, MSMs and FSWs. Evidence support the continued increase of the HIV epidemic among MSMs. In addition to the lack of studies on MSMs and FSWs in the MENA region, our review highlights the lack of data on the practices, characteristics, or the status of HIV infection and viral hepatitis among male sex workers selling or exchanging sex for money.

**CONCLUSION:** The MENA countries are in urgent need of advanced research and strengthening of the data collection systems and reporting practices of these infections among key populations.

**Key words:** Human immunodeficiency virus; Hepatitis B virus; Hepatitis C virus; Men who have sex with men; Female sex workers; Injecting drug users; Prisoners

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**Core tip:** Despite the availability of preventive and control measures, co-infection of human immunodeficiency virus (HIV)-positive individuals with hepatitis B virus (HBV) and/or hepatitis C virus (HCV) is a global health problem of significant and increasing magnitude. While the potential of worse HIV outcomes are suggested to be associated with viral hepatitis, it is still yet to identify the populations in the Middle East and North Africa (MENA) region with dual infections (HIV-HBV or HIV-HCV) or triple co-infections with HIV, HBV and HCV. This review highlights the available data on HIV, HBV and HCV and their co-infections in the MENA countries with specific focus on high-risk groups (men who have sex with men, female sex workers, injecting drug users and prisoners).

Melhem NM, Rahhal N, Charide R, Kreidieh K, El-Khatib R. Human immunodeficiency virus and viral hepatitis among high-risk groups: Understanding the knowledge gap in the Middle East and North Africa Region. *World J Hepatol* 2015; 7(25): 2619-2630 Available from: URL: <http://www.wjgnet.com/1948-5182/full/v7/i25/2619.htm> DOI: <http://dx.doi.org/10.4254/wjh.v7.i25.2619>

## INTRODUCTION

In 2013, 35 million people were estimated to be living with human immunodeficiency virus type-1 (HIV-1). Globally, 2.1 million people became newly infected with HIV in 2013, down from 3.4 million in 2001. Acquired immunodeficiency syndrome (AIDS)-related deaths peaked in 2005 and have fallen by the end of 2013 whereby 1.5 million people died from AIDS-related

causes worldwide compared to 2.4 million in 2005<sup>[1]</sup>. The use of combined antiretroviral therapy (cART) has significantly reduced the mortality and morbidity caused by (HIV-1). In the Middle East and North Africa (MENA) countries, the picture of the HIV-1 epidemic is different. 230 000 people living with HIV were reported in 2013, 15000 deaths and a treatment coverage estimated to be 11% (range of 8%-16%)<sup>[1]</sup>.

Recent data show that liver pathology is a significant cause of morbidity and mortality in HIV patients co-infected with hepatitis B virus (HBV) or hepatitis C virus (HCV). Moreover, HIV-infected individuals do not respond well to treatment for HBV or HCV and hence are at increased risk of hepatic toxicity<sup>[2,3]</sup>. Globally, 240 million people are chronically infected with HBV (defined as hepatitis B surface antigen positive for at least 6 mo) [World Health Organization (WHO)]<sup>[4]</sup>. Data from other sources have reported 350-400 million people infected worldwide with HBV<sup>[3]</sup>. The majority of these cases are in Asia and Africa where HBV is endemic<sup>[5]</sup>. One hundred and thirty-170 million people are infected with HCV<sup>[6]</sup> with 3-4 million people newly infected each year with HCV. These numbers exceed the number of people living HIV-1.

According to the WHO Eastern Mediterranean Regional Office, there are approximately 4.3 million people infected with HBV (1.79% of the global prevalence) and 800000 people infected with HCV in the region (0.57% of the global prevalence) each year<sup>[7]</sup> HIV, HBV and HCV are blood-borne viruses with similar modes of transmission. HIV-1 is mainly a sexually transmitted virus (vaginal or anal sex). HIV-1 can also be transmitted *via* sharing needles or syringes used to prepare injection drugs with someone who is HIV-positive. Similarly, HCV is most commonly transmitted through the sharing of injecting tools; consequently, people at high risk of acquiring HCV include among others people who inject drugs and HIV-infected people<sup>[8]</sup>. While transmission of HBV varies depending on a country level of endemicity<sup>[9]</sup>, injecting drug use has been described as an important mode of transmission among young adults<sup>[10]</sup>. In summary, the categories of people at high risk of acquiring HIV-1, HBV and HCV include commonly: Men who have sex with men (MSMs), female sex workers (FSW), injecting drug users (IDUs) and prisoners engaging in risky behaviors.

Despite the availability of preventive and control measures, co-infection of HIV-positive individuals with HBV and/or HCV is a global health problem of significant and increasing magnitude. Globally, 5%-20% of the HIV-infected individuals are inflicted by chronic hepatitis B and therefore accounting for an estimate of 2 to 4 million<sup>[11]</sup>. In countries where the viruses are highly endemic, the co-infection can reach 25%<sup>[12]</sup>. Worldwide, the burden of HIV-HCV co-infection is estimated to be 4 to 5 million persons<sup>[13]</sup>. While the potential of worse HIV outcomes are suggested to be associated with viral hepatitis, it is still yet to identify the populations in the MENA region with dual infections (HIV-HBV or HIV-HCV) or triple co-

**Table 1** Human immunodeficiency virus, hepatitis B virus and hepatitis C virus and their co-infection status among prisoners from Middle East and North Africa countries between 2005 and 2015

Country	<i>n</i>	Mean age/age	HIV (%)	HBV (%)	HCV (%)	HIV-HBV co-infection (%)	HIV-HCV co-infection (%)	Triple infection (%)	Ref.
Egypt	500	41.0	0.0	9.8	15.8	0.0	0.0	0.0	[14]
Iran	160	16.6	0.6	0.6	NS	0.0	NS	NS	[15]
	392 <sup>a</sup>	35.9	17.0	4.5	80.5	0.8	14.5	0.8	[16]
	358 <sup>b</sup>	34.7	0.0	6.1	8.1	0.0	0.0	0.0	[17]
	163	34.5	0.0	7.4	7.4	0.0	0.0	0.0	[18]
	249 <sup>a</sup>	35.4	15.1	4.7	64.8	1.1	14.3	1.1	[19]
	150 <sup>a</sup>	31.4	42.5	18.9	75.9	NR	NR	NR	[20]
Lebanon	580	31.7	0.2	2.4	3.4	0.0	0.0	0.0	[21]
Libya	6371	> 16	18.2	6.9	23.7	NR	NR	1.5	[22]

<sup>a</sup>Among prisoners who inject drugs; <sup>b</sup>Drug-related convictions; *n*: Sample size; NR: Not reported; NS: Not studied. All numbers were rounded to the nearest 1. HIV: Human immunodeficiency virus; HBV: Hepatitis B virus; HCV: Hepatitis C virus.

infections with HIV, HBV and HCV. This review highlights the available data on HIV, HBV and HCV and their co-infections in the MENA countries with specific focus on high-risk groups. The aim of this review is to identify gaps in the existing knowledge on the interplay between these viruses in the region among MSMs, FSWs, IDUs and prisoners.

## MATERIALS AND METHODS

In an attempt to understand the lack of full spectrum knowledge of the epidemiology of HIV, HBV and HCV and their existing co-infections in MENA countries and specifically in high risk-groups, we performed an extensive literature search on articles studying these viral infections in the 25 countries of the MENA region. These countries include: Algeria, Bahrain, Cyprus, Djibouti, Egypt, Iran, Iraq, Israel, Jordan, Kuwait, Lebanon, Libya, Mauritania, Morocco, Oman, Palestine, Qatar, Saudi Arabia, Somalia, Sudan, Syria, Tunisia, Turkey, United Arab Emirates (UAE) and Yemen. PubMed database was used as the main search engine. The WHO, Centers for Disease Control and Prevention, Joint United Nations Programme on HIV/AIDS (UNAIDS), World Bank and MENA National AIDS Programs websites were also checked for any updated data on the distribution of any of these infections. Case reports, case series, qualitative studies, editorials, commentaries, authors' replies and animal studies were excluded. Original articles and reviews dealing with the prevalence of HIV, HBV and HCV and their co-infection were included. Data on population type, sample size, age and markers of infections were extracted from the relevant studies.

The search was conducted using predefined combination of keywords or terms to select manuscripts and reviews published during the past decade, *i.e.*, between 2005 and 2015. The following keywords were used in order to identify articles studying HIV and HBV or HCV co-infection: "HIV" and "HBV" or "HCV" in combination with each of the 25 different countries of the MENA region. In order to identify the articles on high risk groups and their impact on the epidemiology of HIV, HBV and HCV in the MENA region, the systematic

PubMed search included the combination of the following keywords and each of the MENA countries listed above: (1) "men who have sex with men" or "MSM" or "homosexual" or "gay"; (2) "female sex workers" or "FSW" or "prostitute"; (3) "injecting drug users" or "IDU" or "drug injectors" or "intravenous drug users"; and (4) "prisoners".

## RESULTS

To our knowledge, 52 articles were deemed eligible using our search technique. These articles included published data on markers of HIV, HBV and HCV and their co-infections in the countries of the MENA region during the past decade. Data were available from 12 countries: Cyprus, Egypt, Iran, Israel, Lebanon, Libya, Morocco, Palestine, Saudi Arabia, Sudan, Turkey and Yemen. The data available on HIV, HBV, HCV and their co-infections from these countries are summarized among prisoners (Table 1), FSWs and MSMs (Table 2), IDUs (Table 3) and other defined populations (Table 4). The latter include blood donors, soldiers, HBV patients, non-injecting drug users, waste handlers and hospital patients.

### *Distribution of HIV, HBV, HCV and their co-infection prevalence among prisoners*

Limited data were published on HIV and HBV/HCV co-infections among prisoners in the MENA region. Data from Egypt, Iran, Lebanon and Libya are summarized in Table 1. The majority of the studies originated from Iran and were geographically distributed as follows: three from Northern Iran prisons<sup>[16,17,20]</sup>, two from Center Iran<sup>[15,18]</sup> and one from Southern Iran<sup>[19]</sup>. The number of participants included in these studies ranged between 150 prisoners in one facility in Iran<sup>[20]</sup> to 6371 prisoners participating in the Libyan study<sup>[22]</sup>. Most of these studies were conducted on male prisoners<sup>[14-17,20-22]</sup> and only one study included female prisoners in Iran<sup>[18]</sup>. The mean age of the study participants ranged between 31.4 and 41 years except for one study conducted on juvenile prisoners in Isfahan, Iran (mean age 16.6 years)<sup>[15]</sup>. None of these studies mentioned the reason of imprisonment. These studies could be referred to as

**Table 2 Human immunodeficiency virus, hepatitis B virus and hepatitis C virus and their co-infection status among female sex workers and men who have sex with men in Middle East and North Africa countries between 2005 and 2015**

Country	n	Mean age/age	HIV (%)	HBV (%)	HCV (%)	HIV-HBV co-infection (%)	HIV-HCV co-infection (%)	Triple infection (%)	Ref.
FSWs									
Lebanon	103 <sup>a</sup>	≥ 18	0.0	0.0	0.0	0.0	0.0	0.0	[23]
Libya	69 <sup>a</sup>	≥ 15	10.1	2.9	7.2	0.0	4.3	0.0	[24]
Turkey	130	38.9	0.0	3.1	0.8	0.0	0.0	0.0	[25]
MSM									
Lebanon	101 <sup>a</sup>	≥ 18	1.0	1.0	0.0	0.0	0.0	0.0	[23]
Libya	227 <sup>a</sup>	≥ 15	5.3	3.1	8.4	0.0	4.4	0.0	[24]

<sup>a</sup>Non-adjusted prevalence using respondent-driven sampling method. All numbers were rounded to the nearest 1. HIV: Human immunodeficiency virus; HBV: Hepatitis B virus; HCV: Hepatitis C virus.

**Table 3 Human immunodeficiency virus, hepatitis B virus and hepatitis C virus and their co-infection status among injecting drug users in Middle East and North Africa countries between 2005 and 2015**

Country	n	Mean age/age	HIV (%)	HBV (%)	HCV (%)	HIV-HBV co-infection (%)	HIV-HCV co-infection (%)	Triple infection (%)	Ref.
Cyprus	40	25-31	0.0	0.0	50.0	0.0	0.0	0.0	[27]
Iran	202	-	NR	NS	52.0	NS	9.4	NS	[28]
	417	≥ 17	24.4	NS	80.0	NS	24.0	NS	[29]
	258	28.8	18.8	NS	65.9	NS	NR	NS	[30]
	233	32.3	7.7	22.7	40.3	4.7	6.4	4.7	[31]
	117 <sup>a</sup>	< 30	0.7	0.7	59.0	0.0	0.0	0.0	[32]
	899	33.9	10.7	50.7	34.5	7.8	8.7	6.5	[33]
	100	17-58	19.0	6.0	56.0	NR	15.0	5.0	[34]
	268	37.0	10.8	6.0	39.2	NR	NR	NR	[35]
	153	30.7	5.9	22.9	59.5	2.0	5.2	1.3	[36]
	539	35.3	NR	NR	NR	0.0	1.1	NR	[37]
200	36.5	1.5	4.5	12.0	0.0	0.0	0.0	[38]	
1327	26.5	20.2	NS	13.5	NS	NR	NS	[39]	
518	35.2	15.5	3.7	69.5	0.6	11.2	0.6	[16]	
Israel	743	33.8	1.9	8.6	69.3	NR	NR	NR	[40]
Lebanon	106 <sup>a</sup>	≥ 18	0.9	2.8	52.8	0.0	0.0	0.0	[44]
Libya	328 <sup>a</sup>	≥ 15	87.1	4.5	94.2	4.2	83.2	NR	[41]
Palestine	192	41.3	0.0	2.6	43.8	0.0	0.0	0.0	[42]
Saudi Arabia	297	31.0	0.7	6.1	37.7	NR	NR	NR	[43]

<sup>a</sup>Estimated prevalence using respondent-driven sampling method. All numbers were rounded to the nearest 1. n: Sample size; NR: Not reported; NS: Not studied; HIV: Human immunodeficiency virus; HBV: Hepatitis B virus; HCV: Hepatitis C virus.

seroprevalence studies since enzyme-linked immunosorbent assay and enzyme immunoassay were used to detect antibodies to HIV, HBV and HCV. Few studies reported in addition to anti-hepatitis B surface antigen (HBsAg) titers the levels of HBs Ag as a marker of HBV infection<sup>[17,18]</sup>. We don't have data on the hepatitis B vaccine status of these prisoners, except for one study held in Isfahan (Iran) clearly stating that the prisoners were not vaccinated against HBV<sup>[18]</sup>. It has been noted in four studies that the populations included were not only prisoners but also individuals who inject drugs; those studies were all done in different areas from Iran<sup>[16,17,19,20]</sup>.

The prevalence of HIV among prisoners as reported during the last decade in these countries ranged from 0% to 42.5% with Iran reporting the highest prevalence rate<sup>[20]</sup> followed by Libya (18.2%)<sup>[22]</sup>. It is rather interesting that HIV was not reported in the study held in the Minia governorate, Egypt among a cohort of 500 prisoners in<sup>[14]</sup>. Compared to Egypt, Lebanon and Libya, Iran also reported highest prevalence rates of HBV and HCV at 18.9%<sup>[20]</sup> and 80.5%<sup>[16]</sup>, respectively. Other

studies from Iran reported significantly lower rates of HBV with 0.6% being the lowest<sup>[15]</sup> and 4%-7% reported in other areas<sup>[16-19]</sup>. In general, Table 1 shows that HBV prevalence rates among prisoners ranges between 0.6%<sup>[15]</sup> to 18.9%<sup>[20]</sup> whereas HCV prevalence ranged between 3.4% in Lebanon<sup>[21]</sup> to 80.5% in Iran<sup>[16]</sup>. We similarly assessed the status of co-infection and found that two studies didn't report on the HIV-HBV/HCV co-infection, one from Iran<sup>[20]</sup> and one Libya<sup>[22]</sup>. However, two studies from Iran reported HIV-HBV co-infection rates to be 0.8%<sup>[16]</sup> and 1.1%<sup>[19]</sup>. The other five studies reported a zero co-infection rate. The co-infection prevalence of HIV and HCV was reported in two Iranian studies with an average rate of 14%<sup>[16,19]</sup>. Triple infections of 0.8%, 1.1% and 1.5% were recorded in Iran<sup>[16,19]</sup> and Libya<sup>[22]</sup>. The other studies either reported a 0% rate or did not assess these co-infections (Table 1).

**Distribution of HIV, HBV, HCV and their co-infection status among FSWs and MSMs**

During the past decade, Lebanon, Libya and Turkey

**Table 4** Human immunodeficiency virus, hepatitis B virus and hepatitis C virus and their co-infection status among different populations from Middle East and North Africa countries between 2005 and 2015

Country	n	Mean age/age	HIV (%)	HBV (%)	HCV (%)	HIV-HBV co-infection (%)	HIV-HCV co-infection (%)	Triple infection (%)	Ref.
HIV infected individuals									
Iran	64	-	-	-	-	18.8	NS	NS	[49]
	168	38.7	-	-	-	NS	87.5	NS	[50]
	1338	32-42	-	-	-	NS	78.0	NS	[51]
	106	36.6	-	-	-	20.8	67.0	NR	[52]
	80	37.0	-	-	-	11.3	33.8	25.0	[53]
	130	50.2	-	-	-	11.5	77.0	9.2	[54]
	391	-	-	-	-	14.5	72.0	7.9	[55]
	201	36.0	-	-	-	44.3	67.2	36.3	[56]
	1444	38.4	-	-	-	NS	78.4	NS	[57]
Morocco	503	39.0	-	-	-	29.4	5.4	NR	[58]
Sudan	358	35.0	-	-	-	26.8	NS	NS	[59]
Turkey	949	37.9	-	-	-	0.0	0.9	0.0	[60]
Blood donors									
Cyprus	5057	34.5	0.0	3.0	0.5	0.0	0.0	0.0	[61]
Iran	6499851	-	< 0.1	0.6	0.1	NR	NR	NR	[62]
	2026628	38.0	< 0.1	0.4	0.1	NR	NR	NR	[63]
UAE	592	-	1.2	67.2	31.6	NR	NR	NR	[64]
Others									
Cyprus	12488	34.5	0.0	2.2	0.5	0.0	0.0	0.0	[61]
Iran	264	41.6	0.4	-	4.5	0.4	NR	NR	[65]
	168	33.2	NR	NS	NR	NS	9.5	NS	[50]
	336	28.5	1.5	5.6	4.5	1.2	0.9	0.9	[31]
	379	29.7	4.0	2.9	35.6	0.8	3.4	0.3	[66]
Libya									
General Population	9170	34.0	0.2	3.7	0.9	< 0.1	0.1	< 0.1	[67]
Medical waste handlers	300	-	0.0	2.3	2.7	0.0	0.0	0.0	[68]
Non-Medical waste handlers	300	-	0.0	0.3	0.0	0.0	0.0	0.0	[68]
Turkey									
ER patients	1000	51.7	0.0	5.0	1.8	0.0	0.0	0.0	[69]
In and out-patients	97000-225000	-	0.3	33.9	1.2	NR	NR	NR	[70]

All number were rounded to the nearest 1. n: Sample size; NR: Not reported; NS: Not studied; HIV: Human immunodeficiency virus; HBV: Hepatitis B virus; HCV: Hepatitis C virus.

reported on the prevalence of HIV, HBV, HCV and their co-infection in MSMs and FSWs (Table 2). The age of the participants was reported to be above 15 or 18 years old for FSWs and MSMs in Libya and Lebanon whereas a mean age of 39 years was reported for the participants in the Turkish study on FSWs. The respondent-driven sampling (RDS) method was used to recruit participants (MSMs and FSWs) for the studies from Lebanon and Libya<sup>[23,24]</sup>. The RDS method was used to increase the chances of recruiting hard-to-reach vulnerable populations<sup>[26]</sup>. On the other hand, a cross-sectional study design was reported by Gul *et al.*<sup>[25]</sup> on FSWs in Turkey and recruitment of participants was not addressed in details (a questionnaire was administered). HIV and/or viral hepatitis were not detected in FSWs in Lebanon; whereas 1% out of 101 Lebanese MSM participating in the study reported HIV-1 or HBV but not HCV nor any co-infection, dual or triple<sup>[23]</sup>. This study reported on the prevalence of HIV and HCV through detection of antibodies and that of HBV through the detection of anti-hepatitis B virus core antigen.

When comparing the rates reported in Libya among

FSWs and MSMs, it was clear that HIV-1 was more prevalent among FSWs (10.1%) as compared to MSMs (5.3%). Similar rates were reported for HBV infection (HBsAg) in Libya with 2.9% among FSWs and 3.1% among MSMs (Table 2). HCV was detected among 7.2% of participating FSWs whereas 8.4% was reported among MSMs. Dual HIV-HCV infections were detected among FSWs and MSMs in Libya (4.3% and 4.4%, respectively)<sup>[24]</sup> but not in Lebanon<sup>[23]</sup> and Turkey<sup>[25]</sup>. Triple infections of HIV, HBV and HCV were not detected in FSWs and MSMs in the three countries reporting on these high-risk groups in the region.

#### **Distribution of single, dual and triple HIV, HBV and HCV infections among IDUs**

During the last 10 years, seven out of the 25 MENA countries published data on HIV and viral hepatitis among IDUs (Table 3). The majority of these studies ( $n = 13$ ) were from Iran and were published between 2007 and 2015<sup>[16,28-39]</sup>. The remaining studies originated from Cyprus, Israel, Lebanon, Libya, Palestine and Saudi Arabia<sup>[27,40-44]</sup>. A common feature between the MENA

countries reporting on IDUs (Table 3) is the predominance of male participants<sup>[16,27-44]</sup>. The Iranian studies covered different geographical areas from Iran, with 5 studies performed in Tehran<sup>[16,28-30,33]</sup>, 2 in Isfahan<sup>[32,37]</sup>, 2 in Shiraz<sup>[31,39]</sup>, 2 in Arak<sup>[34,36]</sup>, 1 in Kashan<sup>[38]</sup> and 1 study included Tehran, Mashhad and Shiraz<sup>[35]</sup>, simultaneously. The pool of participants included in these studies had a mean age ranging between 17 and 58 years<sup>[16,28-39]</sup>. The majority of the studies included IDUs between 29 and 37 years of age. The participants were recruited through interviews (structured questionnaires)<sup>[16,28-39]</sup> and rarely through the RDS method to approach potential participants<sup>[32]</sup>. Furthermore, two studies were performed in Drop in Centers<sup>[37,39]</sup>. Drop in centers are institutions providing health related services to reduce harm<sup>[45]</sup>. Zamani *et al.*<sup>[32]</sup> observed that the development of "social networks" is allowing for an increase in sharing of needles in parts of Iran. Seroprevalance data were reported for HIV, HBV and HCV in 11 studies from Iran<sup>[16,28,31,34,36-39]</sup> with the remaining studies reporting HBsAg as a marker of HBV infection along with the seroprevalances of HIV and HCV among the participants<sup>[32,35]</sup>. Interestingly, Honarvar *et al.*<sup>[31]</sup> reported on different behaviors adopted by the IDU population participating in their study. Those behaviors were categorized as follows: Sexual behaviors, condom use in sexual contracts, cigarette smoking, tattooing and cupping<sup>[31]</sup>.

According to Mathers *et al.*<sup>[46]</sup>, 8 out of the 25 MENA countries (Cyprus, Egypt, Israel, Lebanon, Morocco, occupied Palestinian territory, Oman and Tunisia) have needle and syringe programs (NSPs), however the number of IDUs accessing those programs is not up-to-date. While Iran was not part of that study, Des Jarlais *et al.*<sup>[47]</sup> reported that the first NSP established in Iran was in 2003<sup>[48]</sup>. Des Jarlais *et al.*<sup>[47]</sup> showed that the increase of NSPs was associated with a notable decrease in the number of IDUs in Iran. Recent data show that by 2010, Iran reached a number of 637 NSP sites<sup>[47]</sup>.

For ease of the interpretation of the results, we will report the range of single, dual and triple infections as reported in the 7 countries of the MENA region (Table 3). The seroprevalence of HIV ranged between 0% to 87.1%. Cyprus<sup>[27]</sup> and Palestine<sup>[42]</sup> reported the lowest percentages and Libya the highest<sup>[41]</sup>. The RDS method was applied by Mirzoyan *et al.*<sup>[41]</sup> in Tripoli, the capital of Libya. Thus, there is lack of information from other areas. Authors did not also report on the laboratory assays performed to report on HIV, HBV and HCV. Consequently, we could not report especially for hepatitis B whether the reported data are seroprevalence or prevalence/infection data. With regard to the study done in Israel, authors could not conclude on specific results because the majority of the participants were immigrants<sup>[40]</sup>. Similarly, a 0% rate was reported by the Palestinian study (East Jerusalem Governorate); the authors stated that they aimed at estimating HIV related risky behaviors and could not report on the magnitude of the epidemic<sup>[42]</sup>. In Iran, a variable range of HIV-positives was reported with a low of 0.7%<sup>[32]</sup> to a high of 24.4%<sup>[29]</sup>. The majority of

these studies reported though a range between 10% and 24%<sup>[16,30,33-35,39]</sup>. HBV was reported to be less than 10% in Cyprus, Israel, Lebanon, Libya and Palestine (Table 3). In Iran, the range of HBV seroprevalence and infection was variable in different areas, with values of less than 10%<sup>[16,32,34,35,38]</sup>, 23%<sup>[31,36]</sup> and 51%<sup>[33]</sup>. HCV rates were high in Cyprus (50%), Israel (69%), Lebanon (53%), Libya (94%) and Palestine (40%). Variable results were reported in different parts of Iran with the lowest being 12% and 13%; HCV single infections among IDUs in Iran jumped in other studies to above 35% and reached at time 80%.

Few studies reported the co-existence of HIV and HBV among IDUs; these include a rate of 4% in Libya<sup>[41]</sup> as compared to 2%<sup>[36]</sup>, 4.7%<sup>[31]</sup> and 7.8%<sup>[33]</sup> in Iran. Dual HIV-HCV co-infection was not detected in Cyprus<sup>[27]</sup>, Lebanon<sup>[44]</sup> and Palestine<sup>[42]</sup>. The highest HIV-HCV co-infection rate (83.2%) was reported in Libya<sup>[41]</sup> as compared to those of Iran where the highest rate was found to be 24%<sup>[29]</sup>.

Finally, triple infection with HIV, HBV and HCV were either rarely reported or even studied (Israel, Libya, Saudi Arabia and many parts of Iran) or did not exist among IDUs as the case in Cyprus, Lebanon and Palestine (0% triple infections) (Table 3). In Iran, a range of zero<sup>[32,38]</sup> to 6.5% is reported. The latter study included IDUs from Tehran<sup>[33]</sup> where the highest percentage of HIV-HBV co-infection was reported as compared to the rest of the studies in MENA.

### **HIV, HBV, and HCV among populations other than high-risk groups**

Table 4 includes the categories studied for HIV, HBV, HCV and their co-infections in few MENA countries other than the high-risk groups (*i.e.*, MSMs, FSWs, IDUs and prisoners). HBV and HCV were detected in already known HIV positive patients in Iran<sup>[49-57]</sup>, Morocco<sup>[58]</sup>, Sudan<sup>[59]</sup> and Turkey<sup>[60]</sup>. The age of these patients ranged between 35 and 50 years<sup>[51-60]</sup>. The purpose of these studies was stated to be either to study HIV co-infection with HCV<sup>[50]</sup>, HBV<sup>[49]</sup> or triple infection<sup>[51-56]</sup>. Only three intended to assess the risk factors of these dual and triple infections<sup>[54,55,57]</sup>. Iran was again the leading country in the number of published studies on HBV and HCV co-infections. These studies took place in different areas from Iran: Shiraz<sup>[50,51,57]</sup>, Isfahan<sup>[49,54]</sup>, Tehran<sup>[52,56]</sup>, Lorestan<sup>[55]</sup> and Mazandaran<sup>[53]</sup>. Another study had its population come from Shiraz counseling center for behavioral diseases, and the study was a long cohort taking place from 2003-2011<sup>[57]</sup>. The majority of these studies (9 out of the 12) reported results on the HIV infected population were seroprevalance data<sup>[49-53,56-58,60]</sup> while a study from Isfahan and another from Lorestan reported on anti-HIV, anti-HCV and HBsAg<sup>[54,55]</sup>. The purpose of these studies and the recruitment of participants were variably reported (for example HIV-positive patients in one study attended a consultation center for behavioral diseases)<sup>[49]</sup>. The aim of the study by Alipour *et al.*<sup>[50]</sup> was to identify and quantify the risk

factors of HCV transmission in HIV infected persons and their partners. Alipour *et al.*<sup>[50]</sup> documented that HIV was mainly transmitted by intravenous (IV) drugs and blood transfusion. This comes in agreement with two other reports from Iran suggesting that the prominent mode of transmission for HIV was IV drug use<sup>[54,56]</sup>, and the rest came from engaging in risky sexual behaviors, in addition to the majority being associated with prisons<sup>[54]</sup>. In contrast, the Turkish study reported the most common route of HIV and HCV transmission to be heterosexual behavior followed by IV drugs and homosexual practices<sup>[60]</sup>. The rate of HBV infection among HIV-infected individuals ranged from 0% in Turkey<sup>[60]</sup> to 44.3% in Iran<sup>[56]</sup>, whereas HCV prevalence rate ranged from 0.9%<sup>[60]</sup> and 87.5%<sup>[50]</sup>. Triple infection was either not studied or not reported in the majority of the studies. However in Iran, when studied, the rate of triple infection ranged between 9.2% and 36.3%<sup>[54,57]</sup>.

Data on blood donors were extracted from the few published studies performed in Cyprus<sup>[61]</sup>, Tehran-Iran<sup>[62,63]</sup> and UAE<sup>[64]</sup>. The majority of the participants were males whose age ranged between  $\leq 35$  and 38 years<sup>[61-63]</sup>. The study performed in the UAE did not report on the mean age of study participants<sup>[64]</sup>. The data from these countries reported on markers of HIV, HBV and HCV infections. The studies on blood donors included large samples; the studies held in Iran<sup>[63]</sup> and the UAE<sup>[64]</sup> extended over 6 years. Importantly, HIV prevalence was 1.2% in UAE<sup>[64]</sup>, and less than 0.1% in Cyprus and Iran<sup>[61-63]</sup>. Compared to the other studies among blood donors, only the study performed in UAE reported high HBV and HCV infections, 67.2% and 31.6% respectively<sup>[64]</sup>. In Cyprus, HBV infection rate reached 3%<sup>[61]</sup>, while in Iran the rate was less than 1%<sup>[62,63]</sup>. Similarly the HCV infection rate was less than 1% in Cyprus and Iran<sup>[61-63]</sup>. Dual and triple infections were either not reported (Iran, UAE) or were not looked for among participating blood donors (Cyprus)<sup>[61]</sup>. Protection against HBV as detected by anti-HBsAg among blood donors of the UAE was high (67%). Similarly, the rate of HCV among these participants was 31.6% (Table 4).

Low rates of HBV (2.2%) and HCV (0.5%) were reported among 12488 soldiers in Cyprus, no dual or triple infections since no HIV cases were reported<sup>[61]</sup>. Two studies were conducted in Iran where the HIV, HBV and HCV rates were respectively 1.5%, 5.6% and 4.5% among non-injecting drug users<sup>[31]</sup> and 4%, 2.9% and 35.6% among referrals from behavioral counseling centers<sup>[66]</sup>. When HBV-positive patients were tested for HIV, 0.4% of the participants were HIV-positive and 4.5% HCV-positive<sup>[65]</sup>. A 9.5% HIV-HCV co-infection prevalence rate was determined among HIV-infected individuals' partners in an Iranian study<sup>[50]</sup>.

In Libya, a population-based study including nine districts in Tripoli showed that the average prevalence rates of HIV reached 0.2%, whereas HBV and HCV rates reached 3.7% and 0.9% respectively<sup>[67]</sup>. A case-control study in Libya also studied the risk of acquiring

these infections among medical and non-medical waste handlers<sup>[68]</sup>. HIV was not detected among the cases and controls and thus no dual or triple infections<sup>[68]</sup>. Moreover, 2.3% of the medical waste handlers had HBV compared to 0.3% among non-medical waste handlers<sup>[68]</sup>. In the latter, HCV cases were not reported; however 2.7% of the medical waste handlers had HCV<sup>[68]</sup>.

Hospital patients were also part of large size studies reported from Turkey extending for 5 mo<sup>[69]</sup> and 7 years respectively<sup>[70]</sup>. HIV was not detected among patients visiting the emergency room cases; HBV and HCV rates were 5% and 1.8%, respectively<sup>[69]</sup>. In- and outpatients participating in a similar study in Turkey were also assessed for HIV, HBV and HCV infections. 0.3%, 33.9% and 1.2% were reported, respectively. Dual or triple infections were not reported.

## DISCUSSION

Despite the availability of successful prevention and treatment strategies, co-infection of HIV-positive individuals with HBV and HCV remains a global public health problem. This review highlights the data available on HIV, HBV and HCV co-infections among high-risk groups in the MENA region. Globally, the reported prevalence of HIV-HBV and HIV-HCV co-infections vary among studies. This is expected especially due to the changing epidemiology of these viruses across time. It is estimated that the rate of HIV-infected individuals with concurrent chronic HBV infection can reach up to 25%, especially in high endemic areas for both viruses<sup>[12]</sup>. In less endemic areas, *i.e.*, North America, Europe and Australia, HBV and HIV are acquired through sexual transmission or injection-drug use (prevalence rates are less than 10% in these areas) and half of the IDUs are reported to be co-infected with HIV and HBV<sup>[5]</sup>. The prevalence of HIV and HCV co-infections is estimated to be 2%-2.9% (moderate) in many parts of Sub-Saharan Africa and less than 2% in Europe and other developed areas<sup>[13]</sup>. HIV/HCV co-infections among HIV-positives with history of injection drug use is reported to be between 82% and 93%<sup>[71]</sup> and previously reported to range between 72% and 95%<sup>[13]</sup>. Authors observed that MSMs were at lower risks of co-infection despite the fact that HCV epidemics have been described among HIV-infected MSMs; 1%-12% and 9%-27% were reported between MSM and heterosexuals, respectively.

HIV infection is known to negatively affect all phases of the natural history of hepatitis B infection leading to persistent infection, increased cirrhosis, higher liver-associated mortality and increased risk of hepatocellular carcinoma<sup>[12]</sup>. Similarly, viral persistence, increased viral load, rapid progression to end-stage liver disease and fibrosis caused by HCV are negatively impacted by HIV infection<sup>[72]</sup>.

Our review reveals the paucity of epidemiological data for key populations in many countries of the region. Limited number of studies exists in the MENA region on the status of HIV, HBV and HCV and their co-infections

among prisoners, MSMs and FSWs. We also highlight the lack of studies on the prevalence of HIV, HCV and HBV among transgenders. This is alarming especially when MSMs continue to show high burden of HIV prevalence and incidence globally<sup>[73,74]</sup>. Evidence supports the continued increase of the HIV epidemic among MSMs. In high-income countries and despite the success of cART, HIV epidemic trends are decreasing except in MSMs. HIV is estimated to be increasing at 8% among MSMs in the United States per year since 2001. Similarly, the highest rates of HIV infection are in MSMs in much of Africa, Asia and Latin America. Importantly, and by the end of 2011 only 93 out of 196 countries did not report on the prevalence of HIV in MSMs in the past 5 years<sup>[75]</sup>. The UNAIDS reported a pooled HIV prevalence of as low as 3% in the MENA region to as high as 25% in the Caribbean<sup>[76]</sup>. However, Data on MSMs and HIV infections from the Middle East, North Africa and Sub-Saharan Africa were reported to be emerging.

Consequently, data gaps in surveillance are added challenges to understanding the epidemiology of MSMs in the region. This is especially true due to the stigma, discrimination and homophobia associated with this group. An increased risk of unprotected anal intercourse and higher levels of HIV misinformation were associated with homophobia. Discrimination and stigma were also identified as possible barriers for HIV testing and adherence to treatment<sup>[77]</sup>. In addition, criminalization of HIV transmission and male-male sex make it dangerous for affected individuals to release their status and thus reduce the implementation of recommended services<sup>[73]</sup>.

In addition to the lack of studies on MSMs and FSWs in the MENA region, we don't have any study on the practices, characteristics, or the status of HIV infection and viral hepatitis among male sex workers selling or exchanging sex for money. Male sex workers have been ignored globally in the context of HIV/AIDS. Evidence exists that the HIV burden is either sustained or increasing in this population<sup>[78]</sup>. We believe, along with others<sup>[78]</sup>, that this is also a key population at high risk of acquiring and transmitting HIV and viral hepatitis. Global and regional studies on biological, behavioral and structural factors affecting HIV, HBV and HCV are clearly needed.

In 2008, a range of 11-21 million people has been estimated to inject drug in the world<sup>[79]</sup> where data from the Middle East and many countries in Africa were absent. In a more recent review on hepatitis B and C among IDUs, Nelson *et al.*<sup>[80]</sup> reported a range of 6-15 million worldwide with 1.2 million IDUs being HBsAg positive and 6 million being anti-HBC positive. These populations were mainly clustered in the United States, China and Russia. Data from few countries of the MENA region were included in this study (prior to 2009); these include Cyprus, Egypt, Israel, Lebanon, Palestine, Saudi Arabia, Syria and Turkey. Our review shows that not many countries of the MENA region are advocating for research on these viruses among IDUs during the past 10

years (Table 4). Mumtaz *et al.*<sup>[81]</sup> estimated the number of people who inject drugs to be approximately 626000 (33000-1635000) in the MENA with HIV evidence of epidemics in one third of the countries among IDUs. This review highlighted the low levels of condom use, high level of having sex with sex workers as well as the high level of MSMs and sex selling; all of which indicate a high injecting and sexual risk environment. The prevalence of HCV was estimated to range between 31% and 64%.

Our review shows again the scarce number of estimates of single, dual and triple infection among IDUs in the region except for Iran. Iran is the main country in the region with the highest number of IDUs. NSPs are reported to be present in Egypt, Iran, Jordan Israel, Lebanon, Morocco, Oman, Palestine and Tunisia<sup>[82,83]</sup>. Moreover, the lack of opioid substitution therapy was also reported in the MENA countries except for Israel, Iran, Lebanon, Morocco and the UAE. Harm reduction has been described in prisons in Iran where prisoners can access clean injecting equipment. Evidence suggests that injecting equipment are shared in prisons of Jordan, Kuwait and Lebanon.

We believe that it is also important that HIV, HBV and HCV prevention strategies address the vulnerability among women who use or inject drugs. This is critical especially with the reported increase of HIV prevalence among female IDUs as compared to their male counterparts as well as the increased prevalence of HCV among female IDUs and FSWs<sup>[84]</sup>. Policies to reduce discrimination and sex-based violence, police mistreatment, registration of female drug-users and protection of their rights, access to NSPs and access to HIV and viral hepatitis treatment are all needed and not addressed in the MENA region for FSWs.

It is critical to acknowledge that HIV and co-infections with HBV and HCV are major threats among high-risk groups in the MENA region. Several limitations exist in this review while trying to interpret the variable data: (1) the different types of sampling methods and approaches used to recruit participants in different studies; (2) the definition of HIV, HBV, HCV infections and their co-infections; this depends on the sensitivity of the surveillance documenting the mode of acquisition of these viruses; and (3) the lack of data on size estimation of MSMs, FSWs, IDUs and other populations in the region. It is clear that urgent reforms are needed to take place in order to push for extensive and comprehensive research agenda for countries to be informed about the impact of HIV transmission among high-risk groups and the change in the dynamics of the pandemic. Estimates of key populations at high risk including IDUs, FSWs, MSMs and other lesbian, gay, bisexual, transgenders are needed to guide policy makers to understand the magnitude of the problem. Vaccination against hepatitis B to all IDUs must be a priority especially those that are already HCV-positive. HIV testing of these high-risk populations should also be part of the strategic plan in MENA countries. Understanding these gaps is key to strategize surveillance, bio-behavioral surveillance,



interventions and treatment plans.

This review highlights the paucity and the variability of existing data on high-risk groups and the status of HIV, HBV, HCV infections and co-infection in the MENA region. Without addressing the risks of expanding epidemics among high-risk groups, an AIDS free society will remain an illusion. It is obvious that resources need to be allocated to inform strategic planning and policy of the silently creeping waves of HIV and viral hepatitis epidemics among these groups. The MENA countries are in urgent need of advanced research and strengthening of the data collection systems and reporting practices of these infections among key populations. These efforts are critical to ultimately incorporate findings in setting national health policy priorities in the region.

## COMMENTS

### Background

Despite the availability of successful prevention and treatment strategies, co-infection of human immunodeficiency virus (HIV)-positive individuals with hepatitis B virus (HBV) and hepatitis C virus (HCV) remains a global public health problem. This review highlights the data available on HIV, HBV and HCV co-infections among high-risk groups in the Middle East and North Africa (MENA) region. The high-risk groups include men who have sex with men (MSMs), female sex workers (FSW), injecting drug users (IDUs) and prisoners.

### Research frontiers

To the authors' knowledge, this is the first review on the status of co-infection (dual and triple) of HIV-positive individuals with HBV and/or HCV among high-risk groups in the countries of the MENA region.

### Innovations and breakthroughs

The authors' review highlights the paucity and the variability of existing data from the MENA region on HIV, HBV and HCV co-infections among MSMs, FSWs, IDUs and prisoners. This review draws the attention of researchers to the critical need of addressing the gaps in surveillance, the latter being a challenge to understanding the epidemiology of these co-infections among high-risk groups. Advanced research, strengthening of the data collection systems as well as reporting practices and behaviors among high-risk groups are urgently needed.

### Applications

Resources are needed to be allocated to inform strategic planning and policy on HIV and viral hepatitis epidemics among key populations in the MENA region. These efforts are important especially in setting national health policy priorities in the region.

### Terminology

This review summarizes the existing data on the status of co-infections of HIV-1, the causative agent of acquired immunodeficiency syndrome, and viral hepatitis among high-risk groups in the MENA region.

### Peer-review

Melhem *et al* have reviewed the existing data on the prevalence of coinfection of HIV, HBV and HCV in the MENA region, this is really interesting revision of the existing data.

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