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February 20, 2014

Dear Editor,

Kindly find enclosed our revised manuscript in Word format (file name: Assessing the potential for HIV parenteral_revised.doc), along with a point-by-point reply to the reviewers' comments below.

Title: The potential for HIV parenteral transmission in the Middle East and North Africa: An analysis using hepatitis C virus as a proxy biomarker

Author: Yousra A. Mohamoud, F. DeWolfe Miller and Laith J. Abu-Raddad

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 8061

We would like to thank you and the reviewers for your valuable feedback and suggestions, and the critical appraisal of our work. This input has enriched our article. In this revised version of the manuscript, and in our reply to the reviewers, we have addressed each of the reviewers' comments and suggestions, and would be pleased to accommodate any other, should the reviewers or editor have any further suggestions.

We thank you for your time and consideration.

Yours sincerely,

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The potential for HIV parenteral transmission in the Middle East and North Africa: using hepatitis C virus as a proxy biomarker

Yousra A. Mohamoud, F. DeWolfe Miller and Laith J. Abu-Raddad
REPLY TO REVIEWERS' COMMENTS

We thank the reviewers for assessing our work and for the valuable feedback and suggestions. Please find below a point-by-point reply that addresses each of the reviewers' comments. We have also incorporated these suggestions in the revised manuscript as noted below. We would be pleased to address any further points that the editor or reviewers may find unsatisfactory.

Note: All references to the revised manuscript pertain to the marked copy of this file (found below) including changes implemented through "track changes".

Reviewers' comments

Reviewer #1:

Mohamoud et al. compared with the prevalence of HCV infection data between general population and high risk population groups to assess the potential for HIV parenteral transmission in MENA. They concluded that it should be need to be implemented to avoid the unnecessary spread of HIV, HCV, and other blood-borne pathogens along the parenteral modes of transmission. This seems an important issue in this field.

We thank the reviewer for the thorough review of our work and the constructive feedback. We also appreciate the reviewer's valuable suggestions and comments that have enriched this article. Kindly find below our detailed replies addressing the reviewer's comments.

- 1) Table 1 shows the prevalence of HCV, however, this reviewer wants to ask the authors how the detection methods: HCV RNA by RT-PCR or anti-HCV antibodies by ELISA? There are the same questions in Tables 2 and 3.*

We thank the reviewer for this comment, and recognize that this is a salient issue which needs clarification. All prevalence measures included in this review were from studies which measured hepatitis C virus (HCV) prevalence based on the presence of anti-HCV antibodies. To clarify this in the manuscript we updated the "Prevalence (%)" heading in Table 1, Table 2 and Table 3 to read "Seroprevalence (%)". We have also clarified in two instances, in the abstract and introduction, that we are discussing here antibody prevalence.

- 2) *In Abstract,, we use the prevalence of HCV infection data among general population and...? Relatively low prevalence of HCV infection in the general population.....*

We have corrected the sentence as the reviewer suggested by clarifying the prevalence in the abstract as “HCV infection” (Page 10, Abstract). Specifically the two sentences now read:

“Relatively low prevalence of HCV infection in the general population groups was reported in most MENA countries indicating that parenteral HIV transmission at endemic levels does not appear to be a cause for concern.”

- 3) *In Introduction section,human immunodeficiency virus (HIV); acquired immune deficiency syndrome (AIDS).*

We thank the reviewer for this suggestion. We have defined the acronyms in the introduction (Page 11, Paragraph 3). Specifically the paragraph now reads:

“These include the world’s largest iatrogenic transmission of a blood-borne pathogen; the hepatitis C virus (HCV) epidemic in Egypt during the era of parenteral antischistosomal therapy (PAT)^[1], and two human immunodeficiency virus (HIV) outbreaks in renal dialysis centers also in Egypt^[2, 3]. The region has also witnessed the largest documented nosocomial outbreak in HIV and acquired immune deficiency syndrome (AIDS) history which occurred in a children’s hospital in Libya and involved 402 children, 19 mothers (through breast feeding), and two nurses^[4-6].”

- 4) *Authors may mention about the prevalence of HBV in Discussion section.*

We thank the reviewer for this insightful comment. We have modified the text (Page 17, Paragraph 3) in the revised manuscript to cite the exact proportions of incident HBV and HCV infections in MENA that are attributable to contaminated injections. The paragraph now states:

“While there is a very limited risk for sustainable HIV transmission, there remains a concern for other blood-borne and nosocomial infections. MENA has the highest levels of all regions in the proportion of incident HBV (58.3%) and HCV infections (81.7%) that is attributable to contaminated injections^[7]. Every year in MENA, contaminated injections appear to be the cause of 2.5 million HBV infection, 645,000 HCV infections, and 2,200 HIV infections^[7].”

Additionally, we elaborated on the reduction in HBV prevalence among blood donors in the region in the revised manuscript (Page 18, Paragraph 1). Specifically the paragraph now reads:

“HBV prevalence among blood donors in Turkey fell from 5.98% in 1987 to 2.07% in 2003^[116]. Similarly, in Iran HBV prevalence decreased from 3.4-3.5% in 1979-80 to 0.61% in 2005-06^[44]. In Egypt, 95% of women in the 2005 Demographic and Health Survey reported that the medical provider followed basic injection safety procedures^[8].”

5) *Authors should discuss about the HCV genotypes in this area.*

We thank the reviewer for the valuable suggestion. We have modified the text (Page 17, Paragraph 2) in the revised manuscript to discuss the variability in the distribution of HCV genotypes in the region and the implications of this heterogeneity on our assessment of the potential for HIV parenteral transmission. The paragraph now states:

“While HCV genotype 4 is the most prevalent in Egypt^[9], HCV genotype distribution varies between countries and within countries in the rest of the MENA region. Different HCV genotypes may have different transmission probabilities. This suggests that our ability to use HCV prevalence as a proxy for potential HIV parenteral transmission may be dependent on which genotype is prevalent in MENA countries. However, in their study, Vickerman *et al.* demonstrated that this does not appear to be the case^[10-15].”

Reviewer #2:

It is a research work with an acceptable content, given the lack of scientific publications in all MENA countries. It is most often retrospective studies, do not meet the epidemiological criteria themselves. There is no novelty or innovation. However, the manuscript is clear, easy and enjoyable to read. The Research Ethics has been respected.

We thank the reviewer for the thorough review of our work and the constructive feedback. We also appreciate the reviewer’s valuable suggestions and comments. Kindly find below our detailed replies addressing the reviewer’s comments.

SPECIFIC COMMENTS

The title reflects the subject and details the contents of the main study.

The summary reports clearly background research with defined goals, patients and methods, results argued by studies and a conclusion.

Materials and methods: on the material plane, it is an assessment of the risk of HIV transmission from HCV prevalence in different populations of the MENA region. There is no methods or innovative reproducible assessments. There is no statistical study.

Results: The results provide guidance on the risk of HIV based on the prevalence of HCV.

The discussion is well organized, with adequate theoretical analysis and valid conclusions.

References: The references are adequate, relevant and up to date, however, reference 87 should be amended because HCV prevalence of 30% among hemophiliacs in Algeria is the result of the thesis of Dr. Benchikh from the hematology department of Beni Messous in Algiers presented in 2006 and never published. The authors of reference 87 have merely reproduced the level found by Dr. Benchikh.

The tables reflect the main findings of the study, and are presented appropriately.

personal comments

For information; in the Algerian blood donor (340,000 donations per year), HCV prevalence was estimated in the order of 0.21 % in 2009 and 2010.

In hemodialysis Algerians, HCV prevalence approximately 45 % in 1995 was reduced to 23.8 % (national survey conducted in 9700 patients in 2008).

We thank the reviewer for his valuable feedback on the different parts of this manuscript. Regarding the reviewer's comment on reference 87, we are a little confused. It is our understanding that reference 87 by Saidane et al. entitled "Various complications in haemophiliacs managed by Hospital University of Batna, Algeria" refers to a specific hemophiliac population managed by the hematology department at the University Hospital Ibn Flis Touhami of Batna, in Batna, Algeria. This study was conducted recently, January 2010 to January 2011, and was published in 2011 as an abstract in the Journal of Thrombosis and Haemostasis. It appears to us that the reviewer is referring to a different reference, a study conducted by Dr. Benchikh in the hematology department of Beni Messous, Algeria in 2006. Is this correct? In that case, could the reviewer kindly provide us with the exact reference for this study, and for the two studies mentioned by the reviewer in the personal comments section so we can include them in our review?

Editor's track changes comments:

1) We thank the editor for his suggestions. We have cut down in the number of words in the title to 23 words, but were unable to bring them down to less than 12 words, as requested, while preserving the titles meaningfulness. We would like to request that the editor keep the title as it is, if possible. However, if this request is not feasible we will be happy to take a second attempt at cutting down the title.

2) As requested, all of the editor's other formatting comments have been addressed and changes incorporated in the revised document. PMIDs and DOIs have been added to references with this information available. For most of the studies with no PMID available we have prepared scans of the first pages of these documents and compiled them in one PDF. However, we were unable to find the appropriate location to upload this document in the re-submission link. We will be happy to provide this document when needed.

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~~Assessing the~~**The potential for HIV parenteral transmission in the Middle East and North Africa: An analysis using hepatitis C virus as a proxy biomarker**

批注 [a1]: Title should be less than 12 words.

Running head: Potential for HIV parenteral transmission in MENA

Yousra A. ~~Mohamoud~~¹**Mohamoud**, F. DeWolfe ~~Miller~~²**Miller**, and Laith J. Abu-Raddad^{1, 3, 4}

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批注 [a2]: Author names should be given first, then the complete name of institution, city, province and postcode.

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

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Author contributions:

批注 [a3]: The format of this section should be like this:
Author contributions: Wang CL and Liang L contributed equally to this work; Wang CL, Liang L, Fu JF, Zou CC, Hong F and Wu XM designed research; Wang CL, Zou CC, Hong F and Wu XM performed research; Xue Jz and Lu JR contributed new reagents/analytic tools; Wang CL, Liang L and Fu JF analyzed data; and Wang CL, Liang L and Fu JF wrote the paper.

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Abstract

The Middle East and North Africa (MENA) region has endured several major events of parenteral transmission. Recent work has established the utility of using hepatitis C virus (HCV) as a proxy biomarker for assessing the epidemic potential for HIV parenteral transmission. In this review, we use [HCV data on the prevalence of HCV infection antibody \(seroprevalence\)](#) among general population and high risk population groups to assess the potential for HIV parenteral transmission in MENA. Relatively low [HCV prevalence of HCV infection](#) in the general population groups was reported in most MENA countries indicating that parenteral HIV transmission at endemic levels does not appear to be a cause for concern. Nonetheless, there could be opportunities for localized HIV outbreaks and transmission of other blood-borne infections in some settings such as healthcare facilities. Though there have been steady improvements in safety measures related to parenteral modes of transmission in the region, these improvements have not been uniform across all countries. More precautions, including infection control training programs, surveillance systems for nosocomial infections and wider coverage and evaluation of hepatitis B virus immunization programs need to be implemented to avoid the unnecessary spread of HIV, HCV, and other blood-borne pathogens along the parenteral modes of transmission.

Key words:

Core tip:

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批注 [a4]: Please list 5–10 key words for each paper, selected mainly from Index Medicus, which reflect the content of the study. Each key word is separated by a semicolon.

批注 [a5]: Please write a summary of less than 100 words to outline the most innovative and important arguments and core contents in your paper to attract readers.

Key words: [Hepatitis C virus; HIV; parenteral transmission; Middle East and North Africa; proxy biomarker](#)

Core tip: [The Middle East and North Africa \(MENA\) region has witnessed several major events of infection parenteral transmission. Recent studies of hepatitis C virus \(HCV\) epidemiology established the utility of using HCV as a proxy biomarker for assessing the potential for human immunodeficiency virus \(HIV\) parenteral transmission. Building on these novel ideas, we used HCV antibody prevalence data to assess the potential for substantial and/or sustainable HIV parenteral transmission in MENA. We found that HCV prevalence levels are consistent with limited potential for parenteral HIV transmission, but that there could be still opportunities for localized and isolated HIV outbreaks, particularly in formal and informal healthcare settings.](#)

Introduction

The Middle East and North Africa (MENA) region has endured several major events of parenteral transmission of infectious diseases. These include the world's largest iatrogenic transmission of a blood-borne pathogen; the hepatitis C virus (HCV) epidemic in Egypt during the era of parenteral antischistosomal therapy (PAT)^[1], and two [HIV/human immunodeficiency virus \(HIV\)](#) outbreaks in renal dialysis centers also in Egypt^[2, 3]. The region has also witnessed the largest documented nosocomial outbreak in [HIV/AIDS and acquired immune deficiency syndrome \(AIDS\)](#) history which occurred in a children's hospital in Libya and involved 402 children, 19 mothers (through breast feeding), and two nurses^[4-6].

Parenteral transmission of blood-borne pathogens has been documented to occur, particularly in resource-limited settings including different MENA countries^[7, 8]. A few countries in this region such as Afghanistan, Pakistan, Somalia and Yemen, still lack the resources necessary to screen all blood donations and to sterilize medical equipment^[9-15]. Public health systems in these countries are over-stretched leading to some lapses in safety measures^[16]. Standard precautions are not routinely implemented in public and

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even less so in private practices such as among dentists^[17, 18], and in hemodialysis centers^[19].

MENA also suffers from a high prevalence of unnecessary medical injections, unnecessary transfusions, reuse of needles and syringes, and scarifications^[6, 10, 11, 16, 20-24]. At 4.3 per year, this region has the highest rate of injections per person per year of all regions^[25]. Injections are the preferred mode of therapy even when alternative modes are equally effective and available^[26, 27]. Blood transfusions are performed sometimes even without being medically indicated^[28]. A considerable fraction of the population reports such procedures, between 6.7 to 14.2% of diverse population groups in Sudan reported having blood transfusion at least once in their lifetime^[29-39].

HCV, first identified in 1989, is a blood-borne viral infection^[40, 41]. It is primarily transmitted through direct percutaneous exposures to blood such as blood transfusions, sharing of needles, and accidental percutaneous occupational exposures^[42]. HCV is a major cause of chronic liver disease and hepatocellular carcinoma^[43], and is the most prevalent transfusion-transmitted infection^[44]. It is estimated that 130-170 million people worldwide are infected with HCV^[45, 46]^[46].

Both HIV and HCV are transmitted easily through infected needles^[47]. Evidence from needle-stick injury studies suggest that the injection-related transmission probability for HCV is up to 10 times greater than that for HIV^[47, 48]. Building on this, recent work has established the utility of using HCV [antibody](#) prevalence ([seroprevalence](#)) as a powerful proxy biomarker for the potential spread of HIV through the parenteral modes of transmission^[49-54]. Study findings show, for example, that among a population of people who inject drugs (PWID) if HCV prevalence was less than 30%, then HIV prevalence is likely to be negligible^[52-54]. However, if HCV prevalence is greater than 30%, then HIV prevalence would increase progressively with increasing HCV prevalence^[52-54]. Accordingly, based on the epidemiological overlap between these two infections, HCV prevalence can inform the potential for HIV parenteral transmission in a population, and predict the size of a potential HIV epidemic. HCV in this regards is a better proxy

of parenteral transmissions than hepatitis B virus (HBV) which has other non-parenteral major modes of transmission^[55].

Given the history of major events of parenteral transmission of blood-borne pathogens in MENA, and the emerging HIV epidemics among high risk groups^[56-58], questions have risen as to whether there is ongoing parenteral HIV transmission in MENA beyond PWID, and whether such transmission explains a fraction of HIV acquisitions where there are no apparent identifiable risk behaviors^[59]. To address these questions, given limitations on HIV data, we conducted a review of HCV prevalence among general population and high risk population groups in MENA to assess the potential for HIV parenteral transmission in the region.

This review draws on findings from the MENA HIV/ AIDS Synthesis Project, the largest HIV study in MENA to date^[58, 59]. The project consists of a compilation, synthesis, and analysis of available data on HIV, sexually transmitted infections (STIs), and sexual risk behavior across different population groups and the various countries in MENA^[59]. In this review we summarize one aspect of the HIV/ AIDS Synthesis project, which is the effort examining the potential for major HIV parenteral transmission in this region.

HCV prevalence and HIV transmission potential in general population groups in MENA

Table 1 summarizes the outcome of our review of HCV prevalence among general population groups. On the whole, low to intermediate levels of HCV prevalence are found among general population groups in most MENA countries. HCV prevalence among blood donors in Afghanistan ranges between 0.3% and 1.9% and between 0.1% and 2.1% in Iran. The prevalence among pregnant women is less than 1% in most MENA countries. These levels are not dissimilar to those found in the Americas, Asia, and Europe^[60]. These rather low levels imply that there is a low risk for HIV parenteral transmission among general population groups in the region.

Despite the rather low HCV prevalence levels observed in most countries, MENA as a whole appears to have the highest HCV prevalence worldwide^[61]. This is largely due to the contribution of the high prevalence found in heavily affected countries specifically

Egypt^[62, 63] and Pakistan^[64-67]. The Demographic and Health Survey conducted in Egypt in 2008 estimated a prevalence of 14.7% among individuals 15-59 years^[62]. This high level is believed to be a consequence, at least in part, of the world's largest documented iatrogenic transmission of blood-borne pathogens during the era of PAT mass campaigns in Egypt^[1, 68]. From the 1950s to the early 1980s, the Egyptian Ministry of Health led large-scale campaigns to control schistosomiasis^[68]. Millions of people were treated with intravenous injections of tartar emetic, before an oral drug replaced this standard of care across the country in the 1980s^[69]. Reuse of glass syringes and lax sterilization practices during PAT campaigns appear to have caused widespread infection with HCV, such that Egypt today has the world's highest HCV prevalence^[42, 46, 61, 63].

Pakistan appears to also suffer from a high HCV prevalence. A recent meta-analysis pooling 132 studies found HCV prevalence of 3% among blood donors and 4.7% among the general population in Pakistan^[64]. Although the reasons behind the high HCV levels in this country remain not well understood, several studies investigated the risk factors associated with HCV infection. Nosocomial exposures including reuse of needles, medical procedures and blood transfusions were reported to be strongly associated with HCV infection in this country^[70]. Additionally, community exposures through razor sharing and circumcision by barbers were also identified as risk factors^[70]. The high HCV levels and parenteral exposures identified in both Egypt and Pakistan may suggest a potential for some marginal parenteral HIV transmission in these countries.

Parenteral HCV transmission among general population groups in the region appears to be ongoing though largely at low levels. This is highlighted, for example, in studies conducted among children. HCV prevalence among children in Saudi Arabia ranged from 0.1 to 1.8%^[71-73] and as high as 1.5% in Somalia^[74, 75] and 2.1% in Pakistan^[76, 77]. Studies in Egypt suggest that in addition to vertical transmission, children could have been exposed to HCV horizontally, possibly through household exposures^[78-82]. Medical exposures to HCV at a very young age have been also indicated^[83-86]. HCV prevalence levels, however, are too low to be indicative of sustainable HIV parenteral

transmission, as they are much smaller than the ~30% HCV prevalence threshold indicative of considerable potential for HIV parenteral transmission^[52].

HCV prevalence and HIV transmission potential in high risk groups in MENA

There are specific populations at higher risk for HCV and HIV parenteral transmission in MENA. Table 2 summarizes the outcome of our review of HCV prevalence among different populations at higher risk of HCV infection. High HCV prevalence is found among hospitalized and clinical populations, which have experienced various facility-based medical procedures such as hemodialysis patients and multi-transfused patients. A recent study in Algeria found HCV prevalence of 30% among hemophiliacs^[87]. Incidence studies conducted in Tunisia and Morocco estimate fairly high incidence rates for HCV infection among dialysis patients (2.76 and 9.41 per 100 person-years, respectively)^[88, 89]. Multiple studies in the region have found strong correlations between HCV infection and different medical procedures, perinatal care, and dental treatment^[90-98]. Accordingly, exposures in medical care settings could constitute potential avenues for HIV parenteral transmission.

HIV prevalence has been measured and documented among a number of these high risk populations in several MENA countries. Table 3 lists these HIV prevalence measures. High HIV prevalence of 38.5% was reported among children with thalassemia in Qatar. Similarly, HIV prevalence of 4.8% was reported among blood or blood products recipients in Egypt. These studies with high HIV prevalence, however, tend to be old studies, published in the early 1990s, reflecting infections that occurred mainly before improvements in safety precautions and before implementation of stringent blood screening protocols. Meanwhile, the nil prevalence reported in more recent studies conducted in Iran, Jordan, Lebanon and Morocco reflects cross sectional surveys after safety precautions and stringent blood screening have been implemented widely in this region.

Individuals in certain professions could be at higher risk of being infected, or transmitting blood-borne infections, due to exposures to bodily fluids. Occupational injuries among healthcare workers (HCWs) are common in the region. In Morocco,

occupational injuries were found to be at high frequency, though they were found to be rarely declared^[22, 99]. Forty-nine percent of HCWs in Egypt^[19], 58.9% in Morocco^[99], and 45% in Pakistan^[16], reported a needle stick injury in the previous year^[16]. Another such professional category are barbers, who seem to have a five-fold higher HCV prevalence than the general population (5% in Morocco^{[400][100]} and 2.8% in Turkey^[101]). Acquiring HCV infection at barber shops has been reported in Pakistan^[65, 77, 102]. Studies among traditional barbers in Morocco and Pakistan have shown that the risk of blood-borne infections was not known to barbers nor to their customers and that hygiene conditions were deficient^{[400][100, 103]}. This poses a concern with a tradition in MENA of barbers practicing medicine^{[400][100]}.

Prisoners constitute another group at higher risk of HCV infection and transmission in the region. HCV prevalence of 31.4% was reported among prisoners in Egypt^[104], while the prevalence ranged from 30%^[105] to as high as 78%^[106] among prisoners in Iran. This high prevalence suggests that injecting drug use and sharing of injecting and non-injecting utensils is common in prisons.

Some parenteral transmission of HCV in medical settings appears to be ongoing in MENA. This is evidenced by the high HCV prevalence levels reported among thalassemic children and children on hemodialysis. A recent study conducted in 2010, among 692 Egyptian diabetic children with an average age of 10.4 years, reported a prevalence of 2.5%^[86]. Similarly, another study in Saudi Arabia reported a prevalence of 11% among children with cancer undergoing chemotherapy^[71].

Discussion

Given the rather low prevalence of HCV in general population groups in most MENA countries, parenteral HIV transmission at endemic levels does not appear to be a cause for concern. The only possible exceptions are Egypt and Pakistan where higher levels of HCV parenteral transmission appear to be ongoing. However, HCV prevalence in these two countries is still well below the threshold level of 30%, and thus is not sufficient for sustainable parenteral HIV transmission.

Nonetheless, isolated HIV outbreaks in these two countries and in other countries in the region, particularly in healthcare facilities, could still occur as they have occurred in the past. The largest ever HIV/AIDS nosocomial outbreak occurred in a children's hospital in Libya^[4-6]. The first ever documented HIV outbreak in renal dialysis centers occurred in Egypt^[2], which later witnessed a second HIV outbreak in another renal dialysis center^[3]. More recently, a high HIV prevalence of 35.8% was found in a survey of the general population in Gujarat, Pakistan, and apparently it may reflect an HIV parenteral-transmission outbreak related to medical care procedures^[107].

While HCV genotype 4 is the most prevalent in Egypt^[108], HCV genotype distribution varies between countries and within countries in the rest of the MENA region^[108]. Different HCV genotypes may have different transmission probabilities or natural history. This suggests that our ability to use HCV prevalence as a proxy for potential HIV parenteral transmission may be dependent on which genotype is prevalent in MENA countries. However, as demonstrated by Vickerman *et al*, potential differences in the transmission probability or natural history of the different genotypes do not appear to affect the utility of HCV prevalence as a proxy biomarker of HIV parenteral transmission^[49-54].

While there is a very limited risk for sustainable HIV transmission, there remains a concern for other blood-borne and nosocomial infections. MENA has the highest levels of all regions in the proportion of incident HBV (58.3%) and HCV infections (81.7%) that ~~is~~are attributable to contaminated injections^[25]. ~~In Kuwait, hospital acquired infections occurred in 5.1% of all inpatients costing its national healthcare system \$267,000 daily^[108]. Every year in MENA, contaminated injections appear to be the cause of 2.5 million HBV infections, 645,000 HCV infections, and 2,200 HIV infections^[25]. In Kuwait, hospital acquired infections occurred in 5.1% of all inpatients costing its national healthcare system an estimate of \$267,000 daily^[109].~~ More recently, in Saudi Arabia, 8.5% of admitted patients developed nosocomial infections with the rates being highest for nursery (35.8%), intensive care (19.8%), gynecological (16.2%) and surgical (11.7%) patients^{[409][110]}.

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There have been steady improvements in recent years in MENA in infection control and safety measures related to parenteral modes of infection transmission, with only a few countries still lagging in achieving satisfactory standards. HCV prevalence is a proxy for the cumulative risk of parenteral exposures over an extended period of time and thus may not be representative of more recent trends. Improvements in blood safety measures have apparently reduced HIV infections due to contaminated blood in the region from 12.1% of all infections in 1993 to 0.4% in 2003^{[110],[111]}. In Lebanon and Palestine, no new HIV cases through blood transfusion have been detected for several years^{[111],[112],[113]}. In Iran, HCV prevalence among thalassemia patients decreased from 22.8% to 2.6% following the implementation of blood donor screening^{[113],[114]}. ~~Also in Iran, HCV prevalence among hemodialysis patients decreased from 18% in 2001 to 12% in 2006 in one study^[114], and from 14.4% in 1999 to 4.5% in 2006 in another study^[115]. Similar reductions were also achieved for HBV in both Iran and Turkey. Also in Iran, HCV prevalence among hemodialysis patients decreased from 18% in 2001 to 12% in 2006 in one study^[115], and from 14.4% in 1999 to 4.5% in 2006 in another study^[116]. Similar reductions were also achieved for HBV in both Iran and Turkey^[44, 115, 116, 117]. HBV prevalence in Iran decreased from 3.4-3.5% in 1979-80 to 0.61% in 2005-06^[44]. Similarly in Turkey, HBV prevalence among blood donors fell from 5.98% in 1987 to 2.07% in 2003^[116].~~ In Egypt, 95% of women in the 2005 Demographic and Health Survey reported that the medical provider followed basic injection safety procedures^{[117],[118]}. However, these improvements may have not been uniform across MENA. A study in Pakistan suggested an increase in HCV prevalence in recent years^{[118],[119]}. There is evidence of ongoing HCV incidence at dental and medical facilities^[92-95], and at the household and population levels in Egypt^{[119-122],[120-123]}. There appears to be intrafamilial and household clustering of HCV infection in Pakistan^{[123],[124]}. Talaat *et al* reported on an assessment survey of infection control practices conducted in a random selection of healthcare facilities in Egypt^{[108],[109]}. The survey revealed poor concept of infection control in most healthcare settings^{[108],[109]}. Infection control guidelines were not available, efforts to prevent transmission of nosocomial infections were deficient, and

there was a shortage of critical basic supplies such as antiseptics, gloves, masks, gowns and disposable syringes^[108,109].

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There is room for improvement in infection control and safety measures in healthcare settings in MENA. These improvements should be grounded on training and capacity building of infection control staff, the regular monitoring and supervision of infection control programs in healthcare facilities, and the establishment of surveillance systems for hospital acquired infections^{[108, 124][109, 125]}. Additionally, the availability of critical supplies and equipment such as disinfectants and protective barriers is often challenging in settings with limited resources, and need to be improved^{[108, 124][109, 125]}. Budgetary allocations and efficient advanced ordering are necessary to overcome these challenges. Finally, the promotion of occupational safety and health among HCWs is critical to reduce the incidence of unsafe practices and needle stick injuries among this population. This is key as healthcare facilities constitute the main settings of exposure to blood-borne infections.

Conclusion

Some HIV transmission may be present along the same pathways that HCV is using to spread in MENA. However, the parenteral modes of HIV transmission in the region, other than injecting drug use, are not of a scale that can sustain an HIV epidemic. Isolated HIV outbreaks though could still occur in some MENA countries as they have occurred in the past. Despite the steady improvements in infection control and safety measures, there are continued exposures to blood and bodily fluids in MENA countries which poses a concern for the transmission of other blood-borne infections. More precautions, including infection-control training and capacity building, monitoring and supervision of infection control programs, surveillance systems for nosocomial infections, availability of infection control supplies and equipment, in addition to more coverage and evaluation of HBV immunization programs, need to be implemented to avoid the unnecessary spread of HCV, HIV and other blood-borne pathogens along the parenteral modes of transmission.

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AUTHOR'S CONTRIBUTIONS

~~YAM and LJA conducted the literature review and data retrieval. YAM conducted analysis and wrote the first draft of the paper. FDM contributed to the analysis and drafting of the article. LJA conceived and led the design of the study, analysis, and drafting of the article. All authors contributed to discussion of the results and writing of the manuscript.~~

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COMPETING INTERESTS

The authors declare that they have no competing interests.

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Table 1. Hepatitis C virus prevalence among general population groups in the Middle East and North Africa.

Country	Population	Prevalence (%)	Seroprevalence	References
Afghanistan	Blood donors	0.3-1.9		[125, 126][126, 127]
	Pregnant women	0.31		[127][128]
Algeria	Blood donors	0.18		[128][129]
	Pregnant women	0.19-0.63		[128, 129][129, 130]
Bahrain	Blood donors	0.3		[130][131]
Djibouti	Blood donors	0.3		[131][132]
Egypt	Army recruits	22.1		[132][133]
	Blood donors	2.7-26.6		[104, 133-142][134-143]
	Children	2.1-12.1		[85][85, 95, 104, 143-145][144-146]
	Family of HCV positive patients	0-14		[146][147]
	Fire brigade personnel	39		[104]
	General population	10-41.9		[92, 147][48, 148][49]
	Healthy populations	5-46.7		[96, 149-153][150-154]
	National survey	14.7		[62]
	Pregnant	4.3-19		[154-157][155-158]

Country	Population	Prevalence Seroprevalence (%)	References
	women		
	Rural populations	2.7-60	[158-162][159-163]
	Tourism workers	14.3	[163][164]
	Visa applicants	31.5	[164][165]
Iran	Blood donors	0.1-2.1	[114, 165-174][115, 166-172]
	Children	0-0.6	[172, 173][173, 174]
	Family of HCV positive patients	1.3	[174][175]
	General population	0.1-3.1	[175][176]
	Healthy populations	12.3	[176][177]
Iraq	Pregnant women	3.2	[177][178]
Kuwait	Blood donors	0.8-5.4	[178][179]
	Outpatients	1	[179][180]
Lebanon	Blood donors	0.4-0.7	[180-183][181-184]
	General population	0.7	[184][185]
Libya	Blood donors	0.9-6.6	[185-188][186-189]
	Healthy populations	1.6-7.9	[185, 187][186, 188]

Country	Population	Prevalence (%)	Seroprevalence	References
	National survey	1.2		[189] [190]
Morocco	Blood donors	0.2-1.1		[190-193] [191-194]
	Pregnant women	0.5-1		[190, 194] [191, 195]
Oman	Blood donors	0.4-1.5		[195-199] [196-200]
Pakistan	Blood donors	0.5-16		[64, 77, 200-207] [201-208]
	Children	1.7-2.1		[76, 77]
	Family of HCV positive patients	0.4-20.5		[208-210] [209-211]
	General population	4.7-5.4		[64, 77]
	Healthy adults	3		[77]
	Rural populations	4.6-33.7		[66, 67, 123, 211, 212] [124, 212, 213]
	Vaccinated population with smallpox	21		[67]
Palestine	Women	6.7		[211] [212]
	General population	2.2		[147] [148]
Qatar	Blood donors	0.4-2.8		[213, 214] [214, 215]
	General	0.9		[215] [216]

Country	Population	Prevalence (%)	Seroprevalence	References
Saudi Arabia	population			
	Blood donors	0.4-4.6		[73, 216-224 217-225]
	Children	0.1-1.8		[71-73]
	General	1.7-3.6		[225, 226] [226, 227]
	population			
	Outpatients	2.1-22.5		[227] [228]
	Pregnant	0.1-4.6		[73, 228 229, 229 230]
Somalia	women			
	Subjects	5.1		[230] [231]
	tested for			
	HCV			
	Blood donors	0.6		[231] [232]
	Blood donors	2.4		[231] [232]
	and			
Sudan	hospitalized			
	populations			
	Children	0-1.5		[74, 75]
	Healthy	1-6.5		[74, 232 233]
Syria	populations			
	Outpatients	3		[233] [234]
	Pregnant	0.6		[234] [235]
Tunisia	women			
	Blood donors	0.95		[235] [236]
	Blood donors	0.6-1.1		[236, 237] [237, 238]
	General	0.2-1.7		[238-240] [239-241]
	population			

Country	Population	Prevalence (%)	<u>Seroprevalence</u>	References
Turkey	Blood donors	0.2-0.4		[241-246] [242-247]
	Controls	1.3		[247] [248]
	Engaged couples	0.1		[248] [249]
	Family of 2			[249] [250]
	HCV positive patients			
	General population	0.6-2.3		[248, 250, 251] [249, 251, 252]
	Obstetrics and gynecology patients	0.9		[252] [253]
	Outpatients	2.2		[253] [254]
	Rural populations	1		[254] [255]
UAE	Soldiers	0.5-0.6		[244] [245]
	Blood donors	0.5-1.10		[255, 256] [256, 257]
	College students	0-0.4		[257, 258] [258, 259]
Yemen	Blood donors	1.1		[259] [260]
	Healthy populations	2.1-4.2		[260, 261] [261, 262]

*Note: results shown are not of an exhaustive and systematic literature review.

Table 2. Hepatitis C virus (HCV) prevalence among different populations at higher risk of HCV infection in the Middle East and North Africa.

Country	Population	Prevalence e (%)	Seroprevalence (%)	References
Afghanistan	People who inject drugs	36.6		[262][263]
Algeria	Multi-transfused patients	30		[87]
Bahrain	Hemodialysis patients	7.4-9.24		[130, 263][131, 264]
	Multi-transfused patients	40		[264][265]
Egypt	Children with hepatosplenomegaly	16.4		[132][133]
	Chronic liver disease patients	46.2-73.5		[132, 265][133, 266]
	Hepatocellular carcinoma patients	78.5-84		[150, 266][151, 267]
	Healthcare workers	1.4-7.7		[139, 267][140, 268]
	Hemodialysis patients	46.2-100		[132, 139, 145, 268-270][133, 140, 146, 269-271]
	People who inject drugs	63		[148, 271][149, 272]
	Jaundice patients	27.3		[272][273]
	Kidney transplant patients	23.3		[273][274]
	Multi-transfused	11.1-81.6		[8585, 104, 132133, 139140,

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Country	Population	Prevalence e (%)	References
Iran	patients		274-278 275-279
	Prisoners	31.4	[104]
	Sexually transmitted infections patients	5.3	[279] [280]
	Female sex workers	2.7	[280] [281]
	Hepatitis B virus patients	12.3	[281] [282]
	Hemodialysis patients	2.9-55.9	[165, 282-286] [166, 283-287]
	HIV positive patients	11.5	[287] [288]
	Multi-transfused patients	5.1-71.3	[44, 113 , 165 114 , 166 166 , 167 , 173 174 , 284 285 , 288 - 300 289-301]
	Injecting and non- injecting drug users	7.4-80	[105, 106, 169 , 285 , 301 - 306] 170 , 286 , 302 - 307]
	Prisoners	30-78	[105, 106, 304 , 307 , 308] 305 , 308 , 309]
Iraq	HIV positive patients	66	[309] [310]
	Multi-transfused patients	67.3	[310] [311]
Jordan	Multi-transfused patients	40.5	[311] [312]
Kuwait	Hemodialysis	27-40	[312-314] [313-315]

带格式表格

Country	Population	Prevalence e (%)	Sceroprevalence References
	patients		
	Multi-transfused	33	[315][316]
	patients		
Lebanon	Healthcare workers	2.6	[316][317]
	HIV positive	25	[317][318]
	patients		
Libya	Diabetics	24.4	[318][319]
	Healthcare workers	2-6.8	[185, 187, 319][186, 188, 320]
	Hemodialysis	20.5-42.5	[185, 320][186, 321]
	patients		
	Multi-transfused	10.8	[185][186]
	patients		
Morocco	Barbers	1.1-5	[100, 321][100, 322]
	Hemodialysis	10.1-76	[190, 322-324][191, 323-325]
	patients		
	Multi-transfused	2.3-42.4	[190, 323, 325, 326][191, 324, 326, 327]
	patients		
Oman	Hemodialysis	26.5	[195][196]
	patients		
	People who inject drugs	11-53	[327][328]
	Kidney transplant	13.4	[195][196]
	patients		
	Medical students	0	[195][196]
Pakistan	HCC patients	33	[328][329]

带格式表格

Country	Population	Prevalence e (%)	Seroprevalence (%)	References
	Healthcare workers	5.5-31		[77, 329-330, 330-331]
	Hemodialysis patients	68		[65, 334-332]
	Hospital attendees	3.1		[332][333]
	Injecting and non-injecting drug users	22-91		[333-336][334-337]
	Multi-transfused patients	13.2-60.0		[337-339][338-340]
	Patients receiving frequent injections	44		[340][341]
	Type 2 diabetes patients	36		[341][342]
Qatar	Hemodialysis patients	44.6		[342][343]
Saudi Arabia	Cancer patients	11		[71]
	Chronic liver disease patients	63.6		[343][344]
	Healthcare workers	2.2		[344][345]
	Hemodialysis patients	6.9-84.6		[73, 216-217, 225-226, 345-352-346-353]
	Injecting and non-injecting drug users	10.5-74.6		[226, 353, 354][227, 354, 355]
	Multi-transfused patients	4.6-78.6		[228, 355-358][229, 356-359]
	Non-Hodgkins lymphoma patients	21		[359][360]

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Country	Population	Prevalence e (%)	Seroprevalence (%)	References
	Schistosomiasis patients	17.9		[344][345]
Somalia	Chronic liver disease patients	40.3		[232][233]
	Female sex workers, sexually transmitted infection patients, soldiers, Tuberculosis patients	1.8		[360][361]
	Hospitalized patients	2.2		[74]
Sudan	Hemodialysis patients	19-34		[361, 362][362, 363]
	Hospital attendees	0.4		[363][364]
	High schistosomiasis region	2.2		[364][365]
Syria	Female sex workers	1.96		[235][236]
	Healthcare workers	0-6		[365][366]
	Hemodialysis patients	54.4		[366][367]
	People who inject drugs	60.5		[235][236]
Tunisia	Diabetics	1.3		[367][368]

带格式表格

Country	Population	Prevalence e (%)	Seroprevalence (%)	References
	Healthcare workers	1		[368][369]
	Hemodialysis patients	20-46.5		[369-372][370-373]
	HIV positive patients	39.7		[373][374]
	Multi-transfused patients	42-50.5		[374-376][375-377]
Turkey	Barbers	2.8		[101]
	Cancer patients	2.8-5.8		[377-379][378-380]
	Diabetic patients	3.2-20.8		[247, 380][248, 381]
	Female sex workers	0.8		[381][382]
	Healthcare workers	0.3-1.5		[241, 382][242, 383]
	Hemodialysis patients	0-51.2		[380, 382-385][381, 383-386]
	Chronic kidney disease patients	7		[386][387]
	Multi-transfused patients	4-24.4		[382, 387][383, 388]
United Arab Emirates	Hemodialysis patients	24.4		[388][389]
	Multi-transfused patients	18.8		[389][390]
Yemen	Chronic liver disease patients	21.5-37.1		[260, 261][261, 262]
	Healthcare workers	0.5-3.5		[259, 390][260, 391]

*Note: results shown are not of an exhaustive and systematic literature review.

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Table 3. HIV prevalence among high risk HIV parenteral-transmission population groups in the Middle East and North Africa (other than people who inject drugs).

Country	Population	Prevalence (%)	Seroprevalence	References
Bahrain	Children with hereditary hemolytic anemia	1.6		[264][265]
Egypt	Blood or blood products recipients	4.8		[391][392]
	Thalassemia patients	0		[392][393]
	Children with hemophilia	0		[393][394]
Iran	Thalassemia patients	0		[44, 113, 165, 173, 284, 291, 295-298, 394], 114, 166, 174, 285, 292, 296-299, 395]
	Hemophilia patients	0-2.3		[166, 284, 288-291, 294][167, 285, 289-292, 295]
Jordan	Multi-transfused patients	0		[311][312]
Lebanon	Multi-transfused patients	0		[395][396]
Morocco	Hemodialysis patients	0		[323][324]

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Country	Population	Prevalence (%)	Seroprevalence	References
Pakistan	Multi-transfused patients	0.98		[396] [397]
	Hemodialysis patients	0.98		[284] [285]
Qatar	Children with thalassemia	38.5		[397] [398]
Saudi Arabia	Multi-transfused, thalassemia and sickle cell disease patients	1.3		[398] [399]
	Children undergoing cancer therapy	0		[399] [400]
	Hemodialysis patients	0		[400] [401]
Tunisia	Hemodialysis patients	0		[401] [402]
	Hemophiliacs	8.6		[402] [403]

*Note: results shown are not of an exhaustive and systematic literature review.

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